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American Heart Journal

VOL. 53 MAY, 1957 NO. 5

Original Communications

THE SIGNIFICANCE OF LARGE LATERAL AND SMALL HEAD-FOOT WAVES IN THE BALLISTOCARDIOGRAM OF ECTOPIC BEATS

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BROOKLYN, N. Y.

IN THE ballistocardiograms of normal people and of most patients with heart disease, the head-foot forces in systole are much larger than the lateral forces.[1,2] When the aorta is tortuous, the head-foot waves may become very small, and the lateral waves very large during normal expiration. This can be accounted for by the decrease in right ventricular and increase in left ventricular stroke volume occurring in expiration, and by the position of the two outflow tracts, with the aorta pointing more transversely when the diaphragm rises.[1] When large waves are seen during diastole, as with gallop rhythm and with atrial systoles in complete heart block, the forces are usually much greater in the lateral than in the head-foot traces.[3,4] This can be accounted for by the fact that such forces arise at the inflow tract through the A-V orifices, which are directed leftward.

Ectopic beats usually (but not always) produce small forces in the head-foot traces, and these may be associated with lateral waves much larger than those with normal beats or even with the beat following a compensatory pause. When there are ectopic beats at varying intervals after the normal ones, it can be seen that lateral waves are small with short intervals, normal with long intervals, and large at some intermediate intervals. It was felt that an examination of this phenomenon might cast light on the forces normally set in motion at the A-V orifices during ventricular systole, and on the contribution of such forces to the lateral ballistocardiogram.

METHODS

Routine three-plane ballistocardiograms from about 1,000 subjects were examined and 20 showing ectopic beats with interesting changes in the ballistocardiographic waves were subjected to quantitative study. The method of recording was described, and normal variations were discussed elsewhere.[1,2]

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RESULTS

The ratio of premature systolic waves to the normal waves, together with the R-R′ intervals, are given in Table I, which is arranged in order of increasing size of the ratio for the lateral plane. The shortest and longest R-R′ intervals are shown whenever varying lengths occurred. Ten subjects had fixed intervals, 10 had significant variation in R-R′ intervals. Six subjects had mitral stenosis, which retarded ventricular filling. Seven had aortic insufficiency or heart failure, with rapid diastolic filling. Some had second sounds as early as 0.28 sec. after R, others as late as 0.38 sec. The late sounds usually were pulmonic; the earliest were aortic. No attempt was made to determine whether ballistic waves arose in the right or left side, or to use second sound—R′ intervals in evaluating the ballistic forces.

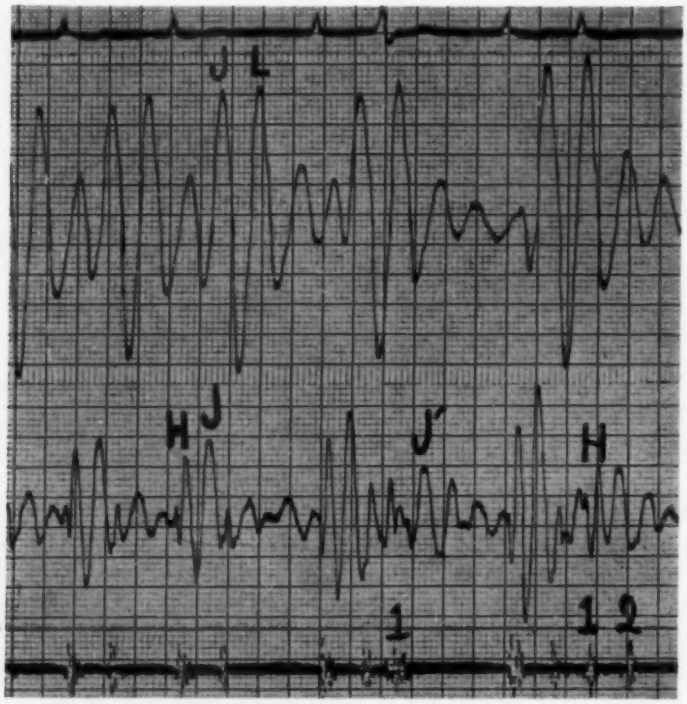

Fig. 1.—Discussion in text. The electrocardiogram, at top, shows an ectopic beat and an early supraventricular beat, the last on the trace. The bottom trace, heart sounds at pulmonic area, shows that the ectopic beat caused no second sound, but that the early supraventricular one has a second sound. Neither of these caused a head-foot complex, both caused small lateral J waves. In all traces, the top ballistic record is the head-foot plane, right-left, and dorsoventral following in that order. Upward on these traces is headward, rightward, or backward.

In Table I, it is apparent that small ballistic head-foot waves are characteristic of ectopic beats, and small lateral waves accompany ectopic beats with R-R′ intervals of 0.4 sec. or less. When R-R′ is over 0.4 sec., the lateral waves due to ectopic beats may be twice as large as normal.

The effects of ectopic beats were studied in a simplified situation in cases of auricular fibrillation with great variation in cycle lengths of the supraventricular beats. In such cases the early supraventricular beats could be compared with equally early ectopic beats. Fig. 1 was taken from a man with mitral stenosis and

TABLE I. RELATIONSHIP OF INTERVAL BETWEEN NORMAL (R) AND ECTOPIC (R′) BEAT AND THE SIZE OF THE SYSTOLIC COMPLEX IN THE HEAD-FOOT AND LATERAL BALLISTOCARDIOGRAM

CASE NUMBER	DISORDER	AGE (YEARS)	R-R′ (SECOND)	HF RATIO	RL RATIO
1304	FM	87	0.38 0.48	0.2 0.6	0.15 0.15
1257	S	12	0.37 0.48	0.25 1.55	0.2 1.25
1267	FM	29	0.42	0.0	0.25
1193	S	37	0.46 0.53	0.15 0.3	0.25 1.0
1006	FM	34	0.46 0.50	0.35 0.5	0.25 0.9
1226	S	69	0.48	0.6	0.25
1507	S	63	0.36 0.45	0.8 0.6	0.25 0.6
704	FM	40	0.38 0.46	0.0 0.4	0.4 1.0
962	FM	60	0.44	0.35	0.6
1262	S	12	0.43 0.48	0.5 1.0	0.7 1.0
1280	S	59	0.42	0.25	0.75
1356	S	22	0.58	1.10	0.80
1383	S	58	0.48	0.4	0.9
1321	S	44	0.46 0.65	0.5 0.65	1.1 1.2
1574	F	63	0.42	0.45	1.2
1475	S	45	0.88	0.6	1.5
1556	S	21	0.56	1.00	1.7
1547	SM	33	0.72	0.6	2.0
1365*	S	49	0.42 0.54	0.50 1.00	2.10 1.00
1678	S	71	0.44 0.52	0.45 0.75	2.5 2.0

F indicates auricular fibrillation; S, sinus rhythm; and M, mitral stenosis. HF ratio gives the amplitude of the head-foot ectopic I-J divided by that of normally activated beats with intersystolic intervals over 0.80 sec. RL ratio does the same with lateral systolic complex which includes H-I plus I-J, since H is often large in lateral traces.

*In this case, discussed in text, the dorsoventral waves are in the RL, the lateral in the HF column.

insufficiency, and very large ballistic waves, due apparently to thiamine deficiency. This patient (1267) had large H-I-J waves in the lateral trace, and huge J-K-L waves in the head-foot trace, when the cycle length was 0.7 sec. or more. When the cycle length was less than 0.44 sec. there was no second sound, and no sign of any head-foot force. A small lateral J wave occurred in such beats, whether ectopic or merely due to early supraventricular activation. When the cycle length was 0.48 sec., a second sound might occur, but no head-foot I-J. The lateral J was still small, but there was an H wave 70 per cent as large as that in the beats after longer diastoles.

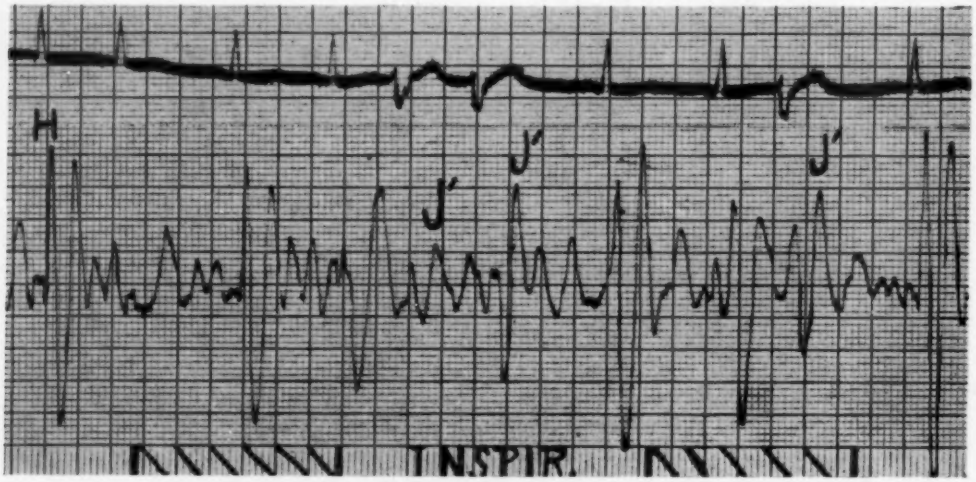

Fig. 2.—Discussion in text. The second beat, supraventricular with R-R = 0.48 sec., does not evoke the huge lateral H-I seen in other beats, but does cause a small broad J wave in the lateral trace. The fifth beat, ectopic, causes only a very small lateral J'. Another ectopic following it causes I'J' of fair size, as does the ectopic beat which is next to last. This one occurs near the end of expiration, when lateral waves normally are largest. The traces in the other two planes also had small J waves with premature beats.

In another case (Case 1304), Fig. 2, a supraventricular beat at 0.40 to 0.44 sec. caused no lateral H or I, and only a small J, if the beat occurred in inspiration. Ectopic beats, during inspiration, at similar periods in diastole, produced identical ballistic patterns. But an ectopic beat as early as 0.36 sec., during expiration, produced lateral H-I-J waves half as large as normal ones. This case shows that the phase of respiration may be critical in determining the size of the lateral ballistocardiogram of ectopic beats.

In Fig. 3, from a man with mitral stenosis (Case 704), early supraventricular activation and a somewhat less premature ectopic beat failed to cause any head-foot force, and produced bizarre lateral J waves, instead of the double rightward wave which coincided with the notched descent of the head-foot I waves when systoles were preceded by longer diastolic intervals. Fig. 4 was obtained from the same patient as in Fig. 3, but after a year of induced hypothyroidism. It is noteworthy that the "mitral notch" on the I wave was altered without valvulotomy. Also, in the right-left trace, a wave synchronous with J, and missing previously, had reappeared in the beats preceded by long diastoles. Again, early ectopic or supraventricular beats failed to cause significant headward

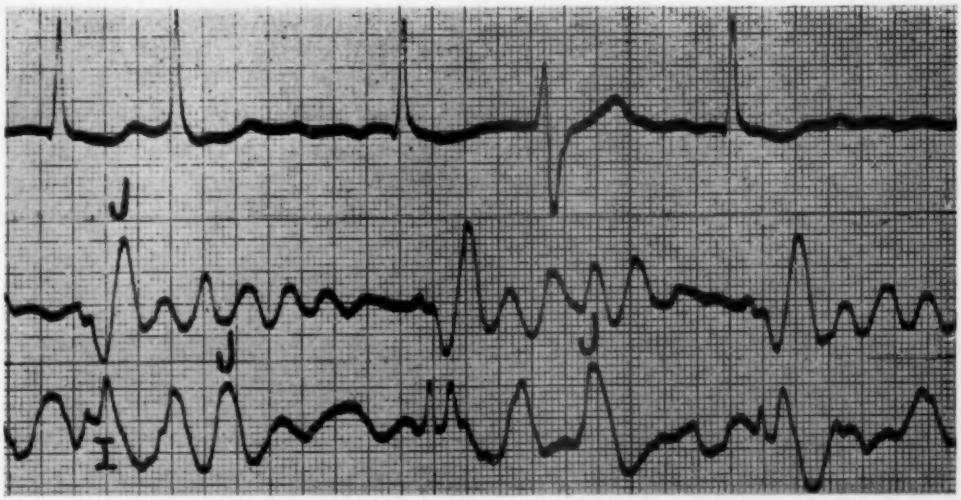

Fig. 3.—Discussion in text. The second and the fourth beats show premature beats, one supraventricular, one ectopic in origin . These beats cause no head-foot motion, but a large lateral J.

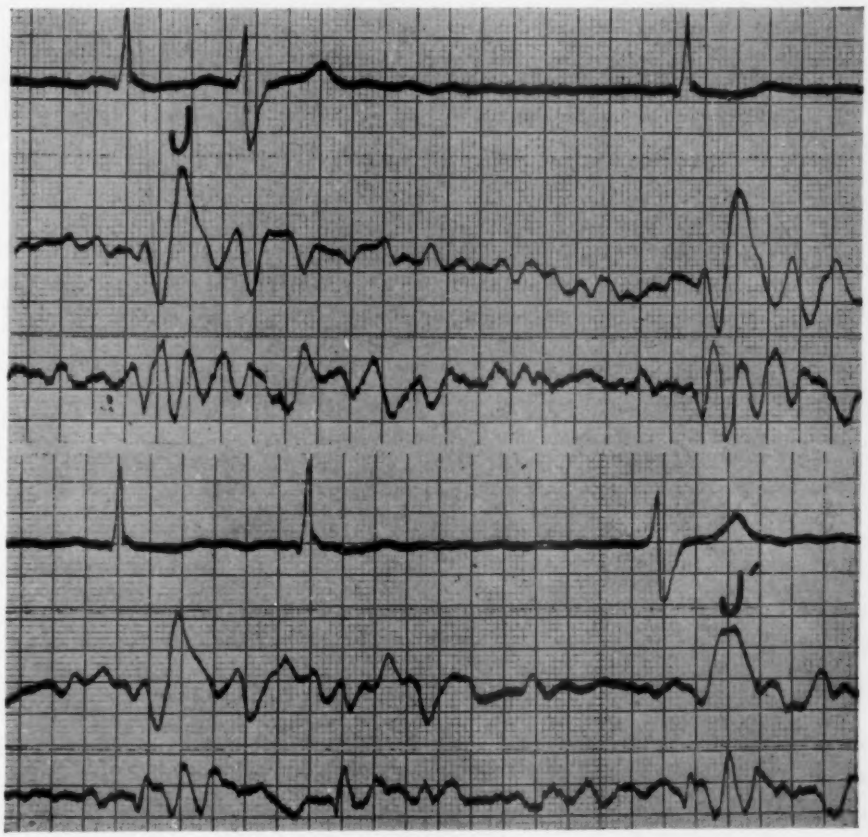

Fig. 4.—Discussion in text. The top set of traces are taken in held expiration, the lower ones in inspiration, with obvious change in lateral pattern, shorter I in head-foot waves. In each set of traces the second beat is early enough to produce minimal ballistic force.

motion and caused no double thrust rightward with the H-I wave, as did beats preceded by long diastoles. An ectopic beat preceded by a long diastole caused a lateral wave pattern like that of supraventricular activation after a long diastole, but the head-foot wave had a short I and broadened J peak, probably due to asynchronous ejection following aberrant activation. All three of these cases are examples of ectopic beats and early supraventricular activation producing identical effects on the ballistocardiogram of fibrillators, and this indicates that prematurity, not aberrant activation, is the important factor in altering the ballistocardiogram of early ectopic beats.

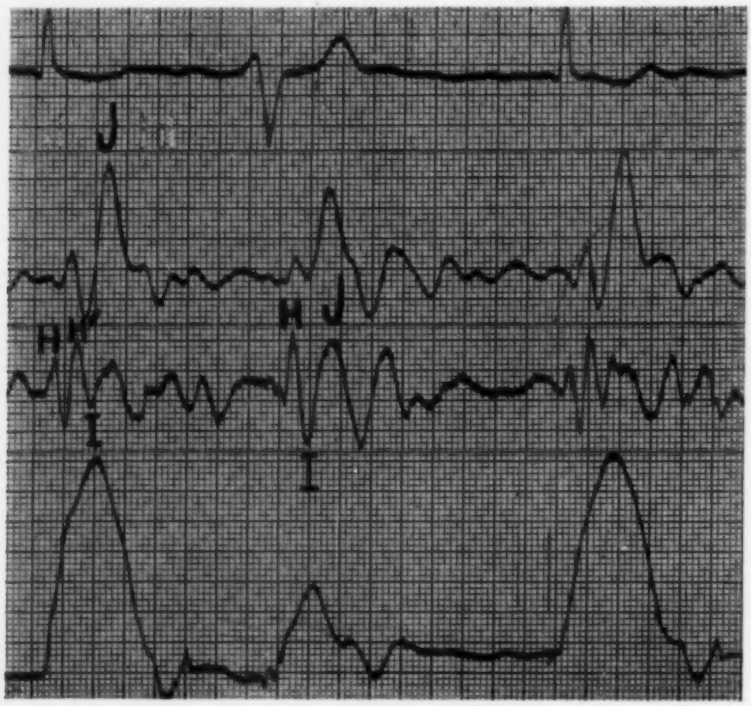

Fig. 5.—Discussion in text. The lower trace is from the carotid artery.

In comparing the amplitude and form of the systolic complexes in ballistocardiograms of supraventricular and ectopic beats, it must be borne in mind that the normal systolic complex is due in part to forces set off by atrial systole. As is apparent in tracings in cases of complete heart block[3] and of wandering pacemaker, the effects of atrial systole are much more evident in the right-left than in the head-foot trace. Hence, with normal P-R intervals, the normal beat will differ from an ectopic ventricular beat in having these atrial elements. Figs. 1 through 4 are from fibrillators; Figs. 5 through 12 are from cases with sinus rhythm.

In striking contrast with the above examples of small lateral waves with early ectopic beats are the examples of abnormally large lateral waves with small head-foot waves after ectopic activation. Thus, Fig. 5, also from a patient with mitral stenosis (Case 1547), shows a small carotid pulse wave, a shortened I wave in the head-foot trace, but very large H, I, and J waves in the right-left

trace due to an ectopic beat with an R-R′ interval of 0.66 sec. Incidentally, this subject had no "mitral" notch on the head-foot I wave, but had a deep notch in the lateral H wave in the beats of supraventricular origin, absent in ectopic beats.

It is only in ectopic beats with R-R′ intervals over 0.5 sec. that large lateral waves are seen in cases of mitral stenosis, while in cases with no mitral disease, they may occur with R-R′ intervals as short as 0.42 sec. Fig. 6, from an elderly woman (Case 1678) with no evidence of hypertension or organic heart disease, shows very large lateral waves with Q-Q intervals of 0.44 sec. Such beats caused

Fig. 6.—Discussion in text. The top set of traces are the heart sounds from cycles like those with the ballistocardiograms below. With Q-Q = 0.41 sec. the first sound is faint; at 0.46 it is loud and there is a second sound, too.

no second sound and very little head-foot motion. Beats only a few hundredths of a second later caused similar lateral waves, but loud first and second sounds and large J waves in the head-foot trace. Unlike those due to normal beats, these J waves were not notched, and the I waves were deep. Thus, aberrant and premature activation caused ballistic waves larger than "normal" beats, probably because there was no atrial interference, and because systole occurred during rapid inflow, which was complete by 0.48 sec. In Fig. 7 (Case 1257), an ectopic beat with R-R′ = 0.38 causes minimal ballistic motion in any plane; but when R-R′ = 0.48 the head-foot I-J is slightly larger and the lateral I-J much larger

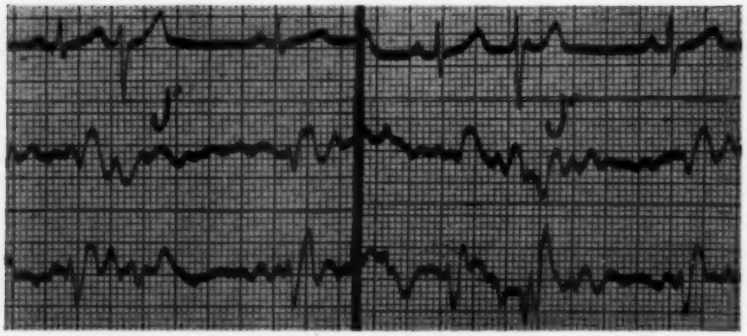

Fig. 7.—From a 12-year-old girl with acute rheumatic fever. Discussion in text.

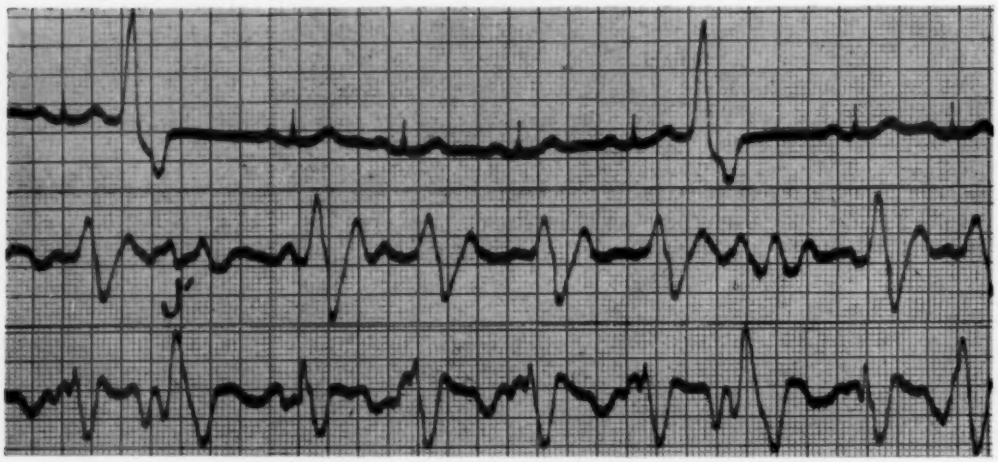

Fig. 8.—Discussion in text.

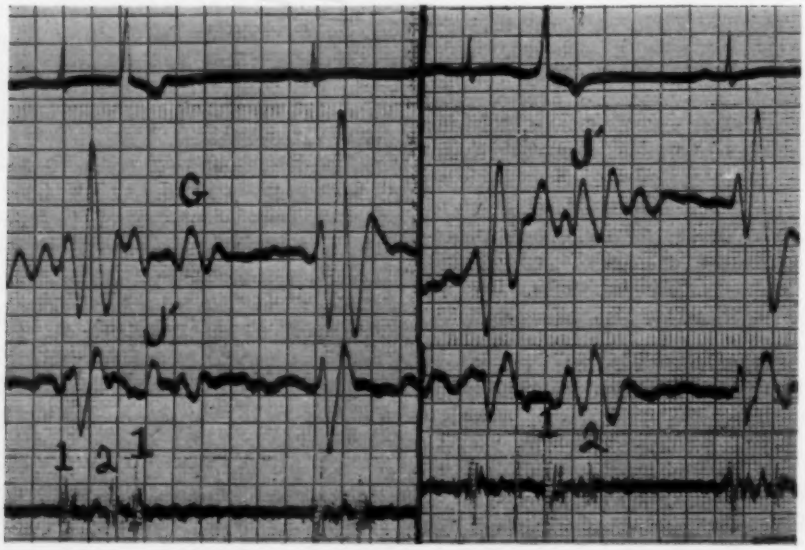

Fig. 9.—Discussion in text. Lower trace is the phonocardiogram with no second sound from the ectopic beat on the left. "Gallop" wave, G, occurs in early diastole.

than with normal beats. Fig. 8 (Case 1383) is a classical example of abnormally large lateral and very small head-foot waves due to ectopic beats at 0.48 sec.

In Fig. 9 (Case 1193), an ectopic beat at 0.46 sec. during held inspiration evoked no second sound, a very small lateral J, and no head-foot J; while the ectopic at 0.52 sec. during normal inspiration produced large lateral waves and first sound vibrations, a faint second sound, and small head-foot I-J complex.

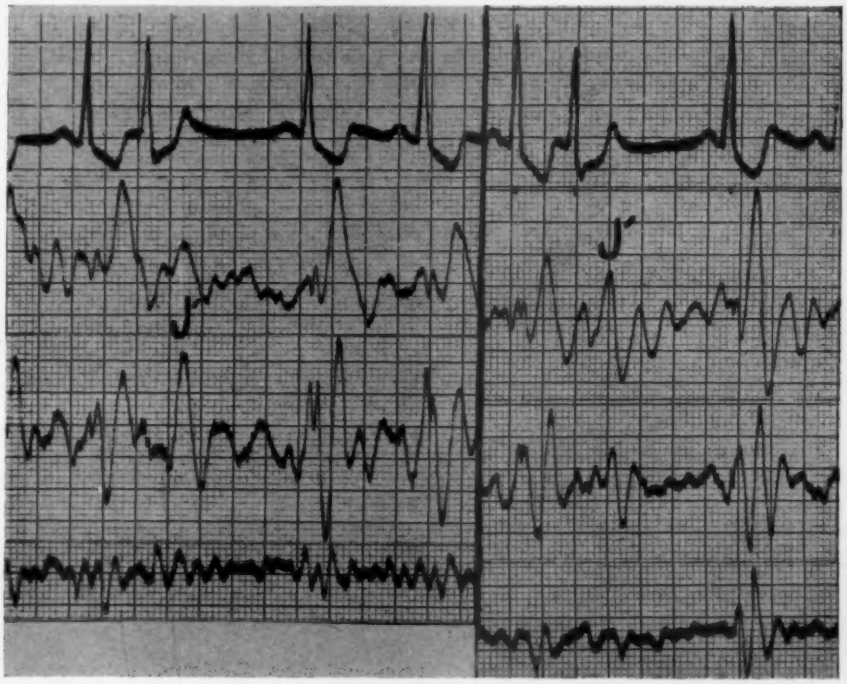

Fig. 10.—Case 1507. Traces on left during held expiration, on right during held inspiration. The lateral I waves and the J from an ectopic beat are large in held expiration; the head-foot ectopic J is larger in held inspiration.

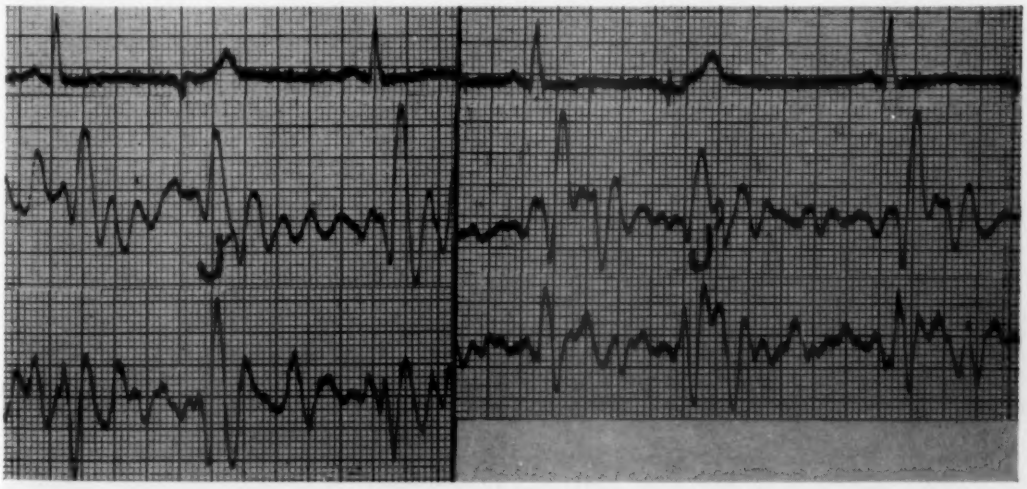

Fig. 11.—Case 1475. Traces on left during held expiration, on right during held inspiration.

Because venous return is such a critical factor, one may observe striking differences in the ballistocardiograms of ectopic beats which follow the same R-R′ intervals, but occur in different phases of respiration. Normally, there is a striking change in the three-plane ballistocardiograms taken in deep inspira-

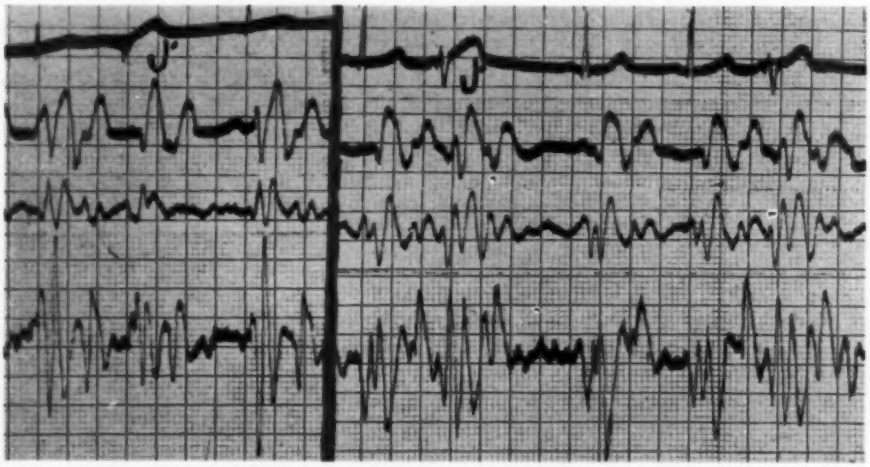

Fig. 12.—Case 1356. Traces on left, held inspiration, with a very large dorsoventral systolic complex in the normal beats (lower trace), and small ectopic dorsoventral and lateral complex with large normal head-foot complex. On right, held expiration. In all planes, ectopic complexes larger than normal ones.

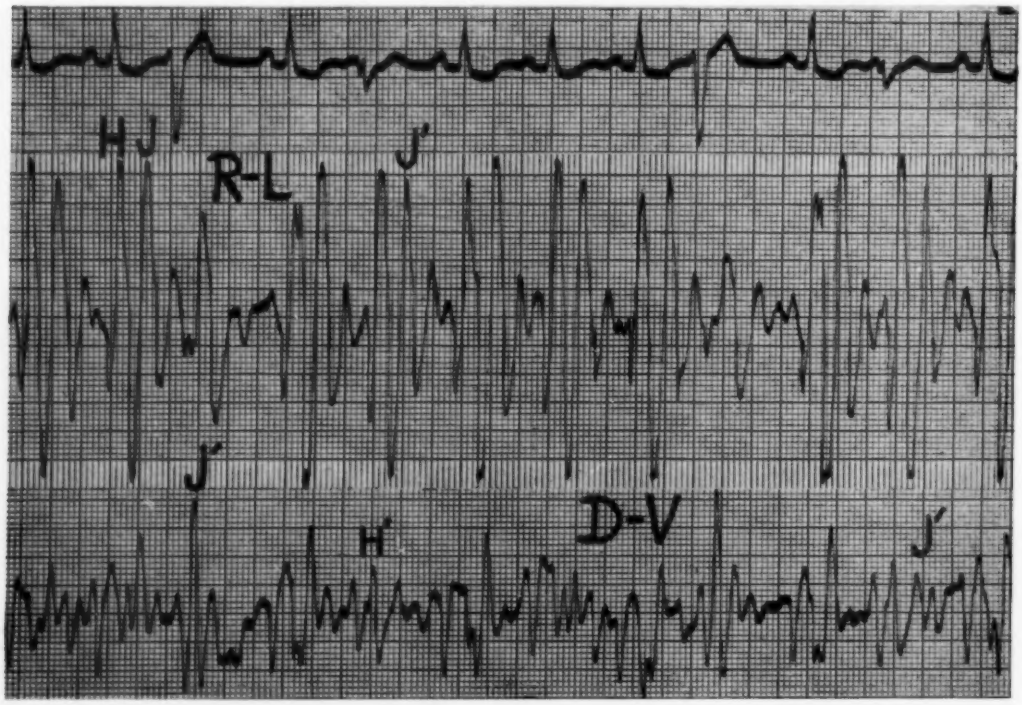

Fig. 13.—From an emphysematous, deep-chested man with aortic insufficiency. Only the lateral and dorsoventral traces are shown; the head-foot trace was a series of small ripples with no systolic or diastolic pattern. The third and ninth beats are ectopic, with R-R′ = 0.36 sec.; the fifth and eleventh beats are ectopic, with R-R′ = 0.50 sec., and they fall 0.12 sec. after P. Discussion in text.

tion and maximal expiration, and in Figs. 10 and 11 it is obvious that, with the same R-R′ intervals, ectopic beats occurring in these two conditions produced very different patterns. These changes may be due partly to a change in position of the A-V septa and the ejection pathways, partly to a difference in velocity of ventricular filling. In Fig. 12 similar changes are seen, but the R-R′ interval is longer with held inspiration, as in Fig. 9.

DISCUSSION

Depending upon the interval (R-R′) between normal and ectopic activation, and on the rate of ventricular filling, an ectopic beat may occur before inflow begins (no first or second sound in such beats), during maximal rate of inflow (loud first sound), or during the initiation or cessation of inflow (faint first sounds). The ectopic beat may occur before either ventricle contains enough blood to permit a pressure rise above that in the great arteries (no second sound in such beats), or when only one ventricle contains enough blood to permit ejection (second sound, but pulsation absent either in the pulmonary artery or in the aorta). This last phenomenon is most often encountered in mitral stenosis, when the right ventricle fills very much faster than the left, and there is a second sound in beats with no carotid pulsation.

The table and figures show that when ectopic beats or premature supraventricular activation in atrial fibrillation cause contraction early in ventricular filling, very small head-foot ballistic forces appear, but the lateral waves may be larger than normal even when the R-R′ interval is as short as 0.42 sec. Such large lateral waves are often associated with abnormally loud first sounds, even when no second sound is evoked. Since there is little or no ejection of blood into the great arteries in such cycles, it seems obvious that the lateral waves arise at the A-V orifices, when inflow is reversed by the ventricular contraction. Later ectopic beats cause larger head-foot and smaller lateral waves. Occasionally, dorsoventral waves vary with lateral waves, but usually they vary with the head-foot waves. The relationship of large lateral and small head-foot waves has been noted previously in the case of atrial beats in heart block and in the waves associated with gallop sounds,[3,4] so that it can be accepted as a general rule that forces associated with ventricular inflow or reflux toward the atria will be much more evident in lateral, and rarely in dorsoventral traces, while those associated with ejection into the arterial bed will be most evident in the head-foot and dorsoventral records.

It has been pointed out previously that lateral systolic waves may be large when the aorta becomes tortuous,[1] and that these waves increase during expiration, when the head-foot waves diminish.[1,2] While this can be accounted for entirely by the known changes in the vector of ejection and the known changes in left and right stroke volume during the respiratory cycle[3] (p. 59 et seq.), it is possible that in heart disease when the largest changes in lateral forces are apt to be seen, there may also be an increase in the systolic force at the mitral valve, and this may contribute to the expiratory increase in lateral systolic waves. Indeed, the chief point emerging from this study of ectopic beats is that it is unwise to assign to the lateral systolic waves any significance in relation

to ventricular ejection, for they may be large during systoles too early or too feeble to cause any ejection of blood and may not change in size when ejection does accompany systole.

In mitral stenosis without right heart failure the lateral waves associated with very early ectopic beats are small. In heart failure without mitral disease even rather early ectopic beats may cause loud first sounds and large lateral waves. The speed of early diastolic filling is maximal in heart failure, with high pressures in the venous systems, and, of course, it is minimal in mitral stenosis combined with tricuspid stenosis. Respiration, by hastening or retarding ventricular filling, also alters the effect of premature beats. The waves are largest when respiration accelerates venous return. Normally, left ventricular filling is augmented by expiration, right ventricular filling by inspiration, and these effects may be exaggerated (pulsus paradoxus) in mild myocardial failure as well as in constrictive pericarditis. In severe failure and in patent ductus arteriosus, the systemic pulse pressure decreases during expiration.[5]

Inspection of the dog's heart and of the human heart beating empty, after occluding venous inflow, and studies of early ectopic beats with the electrokymograph show that considerable change in the shape of the heart occurs with beats which expel no blood into the arteries. Students of the dog's ballistocardiogram report rather large ballistic waves evoked by such beats,[6] presumably due to tugging on the mediastinum, since the chest is open and there is no precordial impulse. An ectopic beat causing a large head-foot ballistic wave was reported in a dog with intact chest.[6] In man, very early ectopic beats and the early beats of supraventricular origin in auricular fibrillation usually cause no head-foot ballistic waves, and lateral waves drop to the vanishing point in beats early enough to cause scarcely perceptible first sounds. Thus, neither mediastinal tugging nor precordial impulses seem to be important contributors to the ballistocardiogram when the human heart contracts so early that ventricular pressures have not fallen below the levels in the atria. The evidence obtained from the study of ectopic beats corroborates that obtained by study of gallop rhythm, wandering pacemaker, and complete heart block, and points to surges of blood, not motion of the ventricular walls, as the source of ballistocardiographic forces in man.

From examination of angiocardiograms it is apparent that the pulmonic outflow tract points dorsally and 5° to 10° to the left of the ventrical axis of the thorax, while the aortic outflow points 20° to 30° to the right of that axis in young people, and over 40° to the right in older people with tortuous aortas and in those with large left ventricles. With right ventricular enlargement or a dilated, tortuous pulmonic artery, there may be marked leftward deviation of the pulmonic outflow tract. These facts are obviously relevant to the amount of vertical, lateral, and dorsoventral force resulting from systolic ejection. Thus, when the outflow is 10° from the vertical, the vertical component is 98.5 per cent, the lateral component 17.4 per cent of the actual thrust; at 30° the corresponding values are 86.6 and 50 per cent; at 45° they are equal at 70 per cent. The rightward deviation of the aorta is so much larger than the leftward deviation of the pulmonary artery that it is not surprising that the head-foot forces normally vary with right venticular ejection, and the lateral forces with left ventricular ejection during respiratory cycles in normal young people.[2]

Examination of angiocardiograms shows that the inflow tracts are directed footward, ventrally, and leftward. Both inflow tracts point in the same direction, and, hence, the lateral forces are not opposed to each other as in the case of the outflow tracts. The leftward deviation is normally 50° or more for both tracts, so that the lateral component should be nearly half again as great as the vertical component with thrusts along these tracts. In ectopic beats with no second sound, where the force apparently all originates at the inflow tract, it is not surprising, therefore, that lateral waves should be relatively large as compared with vertical ones.

In dogs the heart has a very different position in the chest than it does in men. The head-foot component of thrusts along the inflow tract is probably greater than it is in normal men. In disease the shifts in axis of the inflow tract also may be very great in men, but the effect of a deep chest in an emphysematous man is not the same as in the deep-chested normal dog. Head-foot waves are reduced, and dorsoventral waves increased in people with emphysematous chests. Occasionally, such a patient with gallop rhythm will have larger dorsoventral than lateral diastolic waves. One of the patients (Case 1365) with ectopic beats had aortic insufficiency, a tortuous aorta, and marked emphysema. The head-foot trace was a chaotic series of small ripples, but the lateral and dorsoventral traces had large systolic complexes (Fig. 13). With early ectopic beats (R-R′ = 0.36 sec.), the lateral waves were small, the dorsoventral ones much larger than with normal activation. When the ectopic beats occurred much later (R-R′ = 0.50 sec., P-R′ = 0.12 sec., normal P-R = 0.16 sec.), the lateral and dorsoventral waves were similar to normal ones. In this case, the lateral waves reflected force in the tortuous aortic outflow tract, and the dorsoventral waves behaved as though they reflected forces acting at the inflow tract. Presumably, cardiac hypertrophy and emphysema had shifted the axes of both outflow and inflow tracts.

While small ballistic complexes due to ectopic beats have often been described in studies of head-foot traces, no mention seems to have been made of instances, such as seen in Figs. 6, 7, and 12, where the head-foot trace has a deeper I and a sharper and larger J in the ectopic than in the normal beats. So far, we have not noted this in cases of atrial fibrillation, and it seems probable that in these cases waves of atrial origin, out of phase with the I and J waves, deform and reduce the waves in normal beats. Atrial waves are absent in ectopic beats and a normal pattern is revealed. It also is possible that, when the inflow axis permits a large vertical component and the ectopic beat causes a large force along this axis, the head-foot trace is larger and more normal because of this addition to force from the outflow tracts. This does not appear to be the case in these 3 patients, for the lateral waves either are not in phase with the head-foot waves, or no headward wave occurs with large lateral waves, as in the first ectopic beat of Fig. 6.

The facts presented in this study of ectopic beats not only re-emphasize the effect of atrial systole on the I-J waves of the ballistocardiogram, and demonstrate the large element of the lateral systolic complex contributed by motion of blood at the A-V orifices, but they establish also, the absolute necessity of hav-

ing three-plane traces in order to follow the ballistocardiographic phenomena in health and in all abnormalities of cardiac rhythm, valvular structure, or myocardial function.

SUMMARY

Comparison of three-plane ballistocardiograms during supraventricular and ectopic cycles in patients with atrial fibrillation showed that aberrant activation had minimal effect in altering the pattern of ectopic beats, while prematurity had marked and similar effects on ectopic beats and those with normal ventricular activation.

Comparison of ectopic beats and normal beats in sinus rhythm showed that the absence of atrial contraction before ectopic beats contributed to the difference in pattern, but that premature contraction was far more important in determining the change in ballistocardiographic systolic complexes.

Very early beats, which evoked faint first sounds and no second sounds, produced very little ballistocardiographic motion. Somewhat later beats, with normal or loud first sounds, occasionally had lateral systolic complexes larger than normal, although the head-foot complexes and carotid pulse waves were small.

Factors which reduced the rate of return flow to the left ventricle (mitral stenosis; inspiratory phase of normal respiration) prolonged the interval after a normal systole during which premature beats evoked small ballistocardiographic waves, while aortic insufficiency and myocardial failure which hastened early inflow tended to produce short intervals in which small complexes were seen.

These phenomena are interpreted as meaning that motion of blood, rather than motion of ventricular muscle masses, is responsible for almost all the ballistocardiographic force, and that motion of blood at the A-V orifices contributes greatly to the genesis of the lateral forces recorded during ventricular systole.

It is noted that in 3 cases of sinus rhythm, ventricular ectopic beats with broad QRS complexes produced larger head-foot I-J waves and waves of more normal contour than those evoked by normally activated contractions. This may be due to interference of atrial and ventricular waves in normal beats, and absence of such interference in the ectopic beats.

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GENESIS OF LATE SYSTOLIC AND DIASTOLIC BALLISTIC VIBRATIONS

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INTRODUCTION

ULTRA-LOW-FREQUENCY ballistocardiograms are relatively free of body distortion[1-3] and may be interpreted in terms of specific physiologic events.[3,4] Though the origin of the systolic waves is known,[4] the complex diastolic vibrations are less well understood, and have been largely neglected in ballistocardiographic interpretation. It is therefore the purpose of this report to relate clinical observations and animal experiments bearing on the genesis of the ballistic diastolic complex.

METHODS

All records were made with a modified Wittern ballistocardiograph consisting of a light aluminum frame suspended with two degrees of freedom, and with aperiodic damping to a natural frequency of 0.3 c.p.s. Accelerations in, and 90 degrees to, the platform's long axis were measured directly in the range 0.5 to 25 c.p.s.[5] Blood flow velocity was measured with a new strain gauge flow meter based on the principle of the hydrometric pendulum[4]; flow acceleration was obtained by electrically differentiating the velocity signal.

RESULTS

A. *Normal Timing.*—

The last systolic ballistic deflection coincides with the final limb of the blood acceleration pulse and represents deceleration of the arterial column. The first diastolic motion is synchronous with the second heart sound, with the first deflection of the incisura of the central pressure pulse, and in most instances with the end of the electrocardiographic T wave. It may be smaller or larger than subsequent vibrations, and, aside from forces originated by atrial systole, is the only diastolic wave bearing a constant time relationship to other measured variables.

B. *Behavior of Resonating Fluid Columns.*—

1. *Reaction forces from a closed elastic tube:* Both longitudinal and lateral ballistic forces may be originated by mass movements of fluid in a straight, closed, elastic tube.[4] As fluid is manually injected, a wave front distends the tube asymetrically, and if inflow acceleration is adequate, a measurable reaction

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force is produced by the resulting center of gravity change. It is important that the largest ballistic deflections are observed when the plunger is *rapidly* decelerated by impact with the syringe barrel, suggesting that the oscillations of such an elastic system depend not only on force, but on the time course of its application. Shock artifact and standing wave are absent if the tube is sufficiently underdistended, whereas large vibrations may be produced if intraluminal tension is high. Finally, amplitude and rate of decrement of standing wave and platform motion vary with the coupling of the tube to the platform. The biologic parallels to these observations are described below.

2. *Cadaver injection experiments:* In 3 dead dogs the ballistocardiogram was recorded during manual injection of blood into the aortic arch. The experiments differed from those of Starr[6] using human cadavers chiefly in that blood flow was simultaneously recorded. Inflow acceleration was accompanied by a steady rise in aortic pressure and a simultaneous acceleration of the ballistic platform. As in the model, abrupt deceleration produced a single large deflection in the blood acceleration pulse which coincided with the first and largest of several ballistic and pressure waves. Though manual injection at low "diastolic" pressure accelerated blood and platform, ballistic waves originated by plunger-barrel impact were of small amplitude and highly damped. At high "diastolic" pressure, on the other hand, similar impacts generated a flow-deceleration transient and a series of ballistic vibrations larger than those associated with inflow. Gradual deceleration at high diastolic pressure (manual stop) produced small deflections. Though the behavior of the cadaver as a mechanical system is comparable to that of the model, the physiologic relevance of these experiments must be proved in the living animal.

3. *Effect of aortic insufficiency:* Alexander[7] has shown that the standing wave is abolished in experimental, severe aortic insufficiency, presumably because the central end of the resonator is open. In 3 patients with advanced syphilitic aortic insufficiency, all diastolic waves were small despite marked increase in retrograde volume flow.[8] The aortic second sound was absent in each. Five patients with comparable disease secondary to rheumatic fever had clearly defined aortic second sounds and normal diastolic complexes. It is, therefore, probable that the initial diastolic wave bears the same relationship to aortic valve closure as arterial and ballistic shock artifacts bear to plunger-barrel impact in model and cadaver. Subsequent diastolic waves were absent only in those patients without audible evidence of aortic valve closure. Since these people had unimpaired pulmonary valves, the lesser circulation probably does not contribute significantly to the normal diastolic complex.

4. *Importance of resonator pressure and volume:* Since the standing wave in model and cadaver varies with intraluminal pressure and volume, these factors should similarly alter the diastolic complex.

Rapid exsanguination with the aid of suction permits observation of vigorous contraction with the conduits empty.[4] Diastolic waves are virtually eliminated, and reappear only with reinfusion of sufficient volume to restore a sharp dicrotic notch to the pressure pulse. Similarly, nitroglycerin administered intravenously to anesthetized dogs opens the distal end of the resonator and produces a hypo-

dynamic pressure pulse despite transient increase in stroke volume. Diastolic vibrations are decreased but not eliminated. Comparable changes are produced by the maximal vasodilatation which follows spinal transection at C_2.

In contrast, Neo-Synephrine impedes runoff, raises diastolic pressure and stroke volume, and increases the intensity of the second heart sound. These changes are accompanied by large, repetitive diastolic waves at 3 to 5 cycles per second, particularly in longitudinal records; only the first of these is represented in arterial flow. Both nitroglycerin and Neo-Synephrine alter the human ballistocardiogram as described for dogs.

The amplitude of ballistic diastole may be increased at normal diastolic pressure if the systolic input to the resonator is increased, as in complete heart block and in the augmented beat following a compensatory pause. The increase, however, does not compare with that effected by Neo-Synephrine.

The absolute level of pressure appears less important than the relationship between pressure and vessel elasticity, for under appropriate conditions diastolic waves originate in the lesser circuit. In section B, 3 above normal pulmonary valve closure was said to generate negligible reaction force. This conclusion is supported by the observation that 3 patients with pulmonary stenosis and diminished pulmonic second sounds had normal ballistic diastolic complexes. Since the pulmonary artery is under little tension, branches almost immediately, and has an extremely rapid runoff, significant resonance within it is improbable, and the shock of normal pulmonary valve closure should be minimized. On the other hand, 5 patients with uncomplicated patent ductus arteriosus had loud pulmonic second sounds and large lateral diastolic vibrations which disappeared following corrective surgery (Fig. 1). Because of the fistula between aorta and pulmonary artery, the systemic contribution to ballistic diastole should have been minimized, as in aortic insufficiency or after nitroglycerin. The abnormal vibrations were unrelated to volume flow through the fistula, for they were particularly large in a patient with pulmonary hypertension complicating patent ductus, who showed no mixing of systemic and pulmonary blood. Similar diastolic complexes occur with normal or reduced pulmonary flow in association with mitral stenosis, emphysema, and primary pulmonary hypertension. Note that diastolic waves originating in either aorta or pulmonary artery are chiefly exhibited in the long axis of the vessel concerned.

5. *Role of resonator length:* The ratio of headward to footward blood flow remains practically constant throughout life, despite the enormous increase in aortic length. It is, therefore, important that there is no qualitative difference between the systolic ballistocardiogram of infant, child, or adult.

In contrast, the short resonator of coarctation or aortic thrombosis is associated with a small K wave in standard recordings, and as indicated in Fig. 2,*C*, ultra-low-frequency ballistocardiograms exhibit a comparable abnormality. Excision of the coarcted segment restores the record to normal, and similar reversible changes may be produced in dogs by aortic constriction.

In aortic insufficiency a normal relationship exists between headward and footward systolic forces. Insertion of a Hufnagel valve alters aortic flow and produces a typical coarctation pattern, as illustrated in Figs. 2,*D* and 2,*E*. Adap-

tive hemodynamic changes are accompanied by a progressive return to the preoperative wave form.[8]

Hamilton and his colleagues[12] have shown that the central compression chamber includes vessels arising from the arch as well as the iliacs and femorals. We were fortunate in obtaining ballistocardiograms from a 32-year-old woman with congenital absence of all four extremities, and from a 36-year-old man with congenital absence of the left upper and both lower extremities. Two young men with complete traumatic amputation of both lower limbs were also

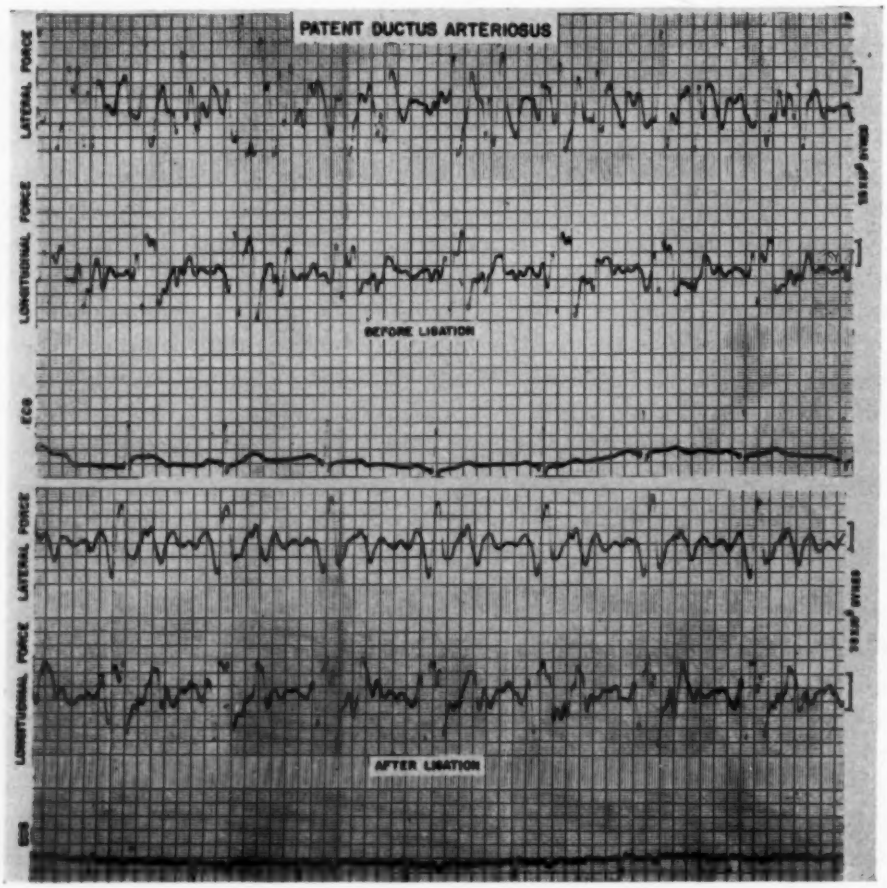

Fig. 1.—Abnormal diastolic waves with pulmonary valve closure in a patient with patent ductus arteriosus. Note that the abnormality is best demonstrated in the lateral record.

studied. All were otherwise healthy, though some degree of atrophy of distal aorta and iliacs probably existed.[13] Late systolic footward force, though reduced, varied markedly in amplitude, while in coarctation it was remarkably constant. Diastolic waves were usually small in coarctation, but in the limbless, prominent repetitive waves at 6 to 10 cycles per second filled diastole. Fig. 2,*F* demonstrates a superimposed vibration cancelling or reinforcing footward systolic force. Note that the distorting vibration is separated from the

first repetitive diastolic wave by an interval precisely equal to the cycle length of the diastolic waves themselves. These ballistic effects cannot be reproduced by inflation of pneumatic cuffs about the limbs of normal subjects, nor are opposite changes observed in exceptionally tall people.

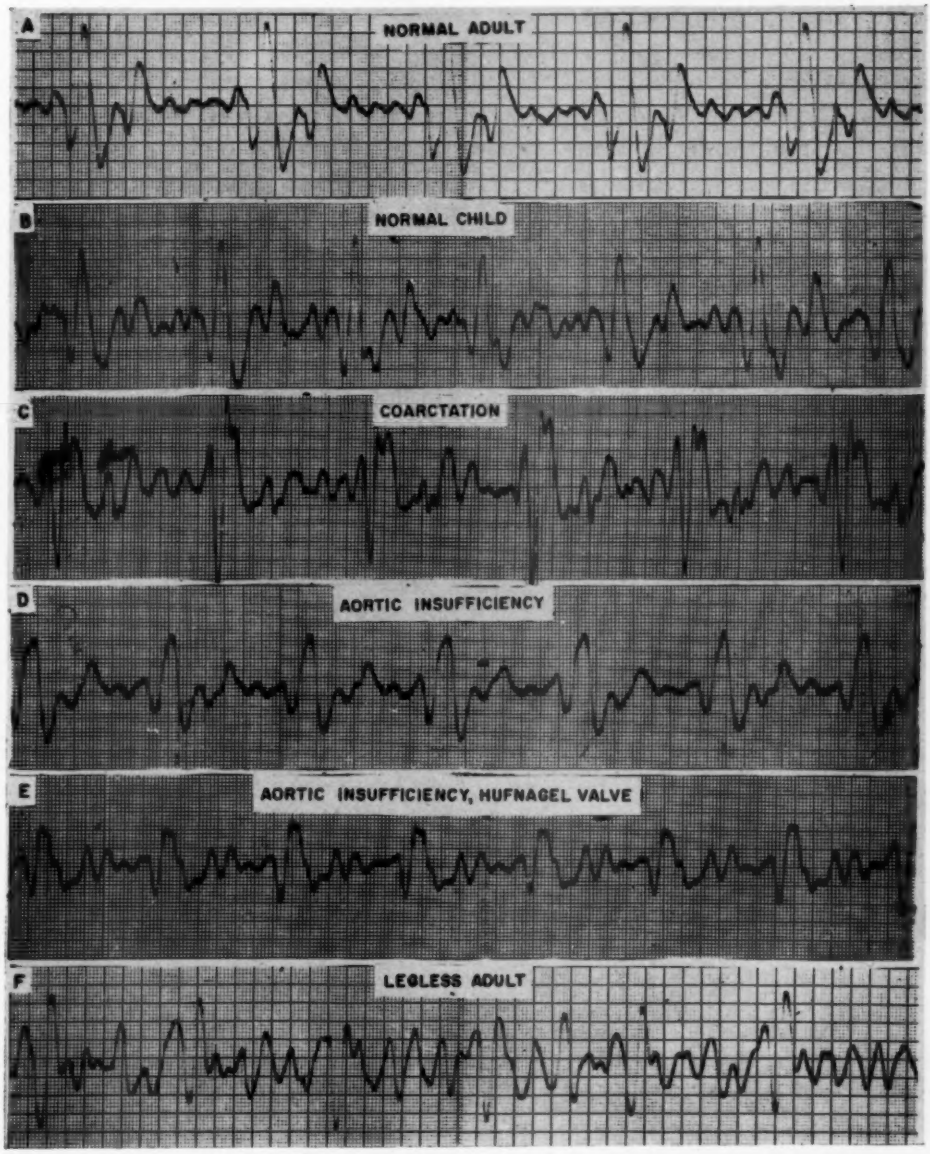

Fig. 2.—The effect of aortic length on the ballistocardiogram. Discussion in text.

6. *Effect of vessel elasticity:* In childhood the standing wave is minimized by all its determinants, and the highly elastic aorta is tightly coupled to the body shell. Ballistic diastolic waves are usually small. Beyond age 40, the aortic coupling loosens as the vessel stiffens, elongates, and bends upon itself.

In the model, loosening the coupling of the tube to the platform permits rolling movements which markedly increase platform motion with the standing wave. Similar diastolic movements of the tortuous aorta are readily demonstrable fluoroscopically, and probably account for the large ballistic diastolic waves characteristic of the elderly.

C. *Importance of Cardiac Motion.*—

The virtual absence of diastolic waves in exsanguinated dogs has been cited in section B, 4. Clamping both aorta and pulmonary artery, complete obstruction of the caval veins, and intravenous air injection also abolish flow and diastolic waves, though cardiac motion persists. Ventricular relaxation fails to displace the body's center of gravity either because it is a symetrical change or because the rate at which it occurs is insufficient to deflect the platform.

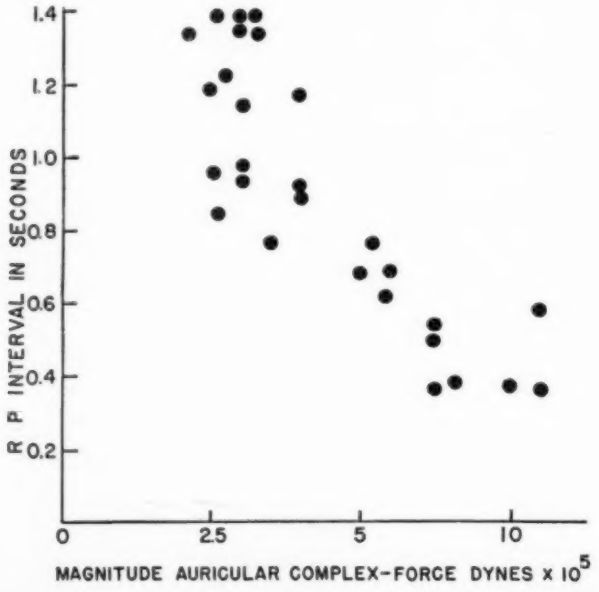

Fig. 3.—The time interval between ventricular and atrial systole in complete heart block, and amplitude of reaction force with atrial contraction. Discussion in text.

D. *Role of Venous Flow and Cardiac Filling.*—

1. *Venous flow:* The caval veins are wide, distensible, valveless structures arranged opposite one another. It is not surprising, therefore, that even in dogs with venous hypertension and reduced systemic flow, high retrograde flow velocities with atrial contraction were unaccompanied by significant reaction forces.

2. *Normal filling:* Though filling cannot be evaluated directly, it seems likely on clinical grounds that neither rapid filling nor atrial contraction normally contribute important diastolic vibrations. The diastolic complexes of patients with and without physiologic third heart sounds are indistinguishable, and in a patient with complete heart block, synchronous atrial and ventricular contraction is not followed by a large diastolic wave, despite somewhat augmented

inflow volume. In the same subject, isolated atrial contraction late in diastole elicits little force, and beats with fortuitously normal time relationships demonstrate that even these small forces are partially superimposed upon early ventricular events.

3. *Increased filling:* In complete heart block, the synergistic effect of atrial contraction during rapid ventricular filling originates large diastolic waves. The amplitude of these vibrations varies inversely and nonlinearly with the interval between ventricular and atrial systole, and therefore with the volume of blood contained in the atrium at the time it contracts (Fig. 3). Similarly, when peripheral venous hypertension and obstruction of venous return are produced by occlusion of the caval veins, sudden release of the obstruction is followed by the appearance of large "V" waves in the atrial pressure pulse and large diastolic ballistic deflections.[4] It is, therefore, probable that when venous inflow is enhanced and/or inflow acceleration increased by venous hypertension and/or atrial systole, intracardiac flow may produce considerable reaction force.

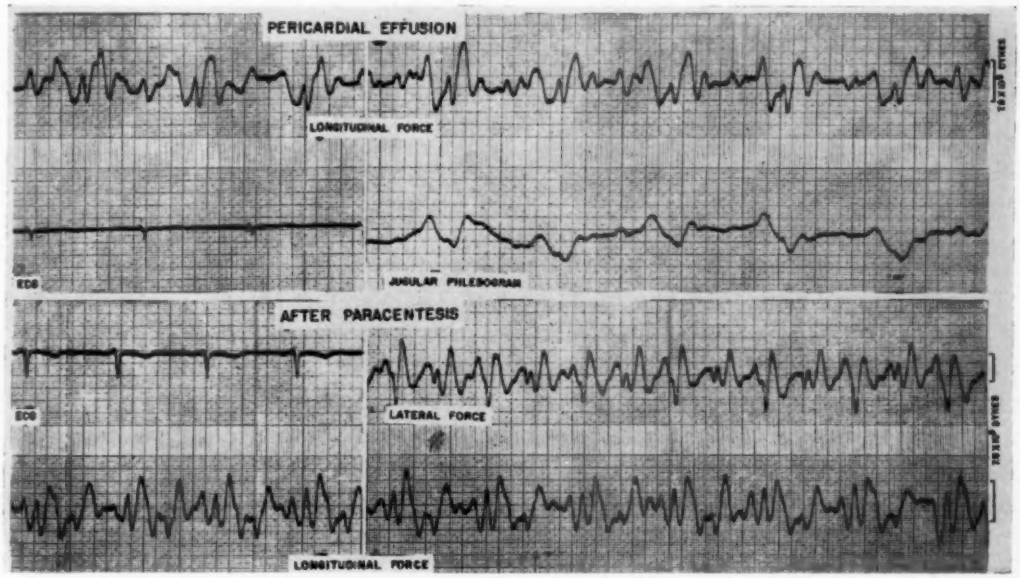

Fig. 4.—Typical diastolic waves with limitation of ventricular expansion. Note that they are synchronous with the "V" wave of the phlebogram, exceed systolic forces in magnitude, and disappear after paracentesis.

4. *Reduced filling:* Most abnormal diastolic waves occur in association with reduced venous return. Patients with pericardial effusion and dogs with hydropericardium exhibit abnormal forces during rapid ventricular filling, and similar ballistic waves occur synchronously with the diastolic "click" of constrictive pericarditis and the protodiastolic gallop of congestive failure. Restoration of normal ventricular expansion by paracentesis, pericardectomy, or reduction of residual volume eliminates the abnormal vibrations. The diastolic waves illustrated in Fig. 4 are typical of the above conditions. The patient is a 16-year-old boy with cardiac tamponade secondary to rheumatic pericarditis.

Similar observations have been reported by other investigators using standard instruments.[14,15] Venous hypertension and sharp arrest of ventricular expansion make for rapid-flow deceleration. It is therefore probable that abnormal ballistic waves with premature cessation of filling are analagous to the shock artifacts of section B, 1 and 2, and are related to rate of change of force (jolt).

DISCUSSION AND CONCLUSIONS

There has been general agreement that the entire ballistocardiogram represented cardiovascular forces, accelerations of heart muscle mass and/or blood. Though this is generally true, the above observations suggest that at least the first time derivative of acceleration is involved in the genesis of some normal and abnormal diastolic waves. Although the ballistocardiogram resembles a phonocardiogram if repeatedly differentiated, ballistic vibrations differ from sound, which is symetrically transmitted and does not displace its source.

With the ultra-low-frequency ballistocardiograph discrete waves dependent upon systolic flow may be identified.[4,5] Though longitudinal platform motion represents the algebraic sum of headward and footward force vectors, systolic deflections related to flow resemble and vary with the simultaneously recorded blood acceleration pulse.[4] Late systolic footward force corresponds to flow deceleration during reduced ejection, and presumably is directed footward because the product of blood mass and deceleration distal to the first intercostal artery exceeds that proximal to the innominate.

Artifact, lack of pulse-wave reflection, decreased aortic length, and abnormal central blood flow all have been suggested to explain the ballistic effects of aortic obstruction.[9,11] The phenomenon is reversible in dog and man, and is demonstrable with ultra-low-frequency instruments which eliminate body distortion and after-fling. The considerable footward force which persists in coarctation despite lack of pulse wave reflection must therefore be considered a forced vibration. A normal relationship between headward and footward force may exist in the absence of a standing wave,[8] and a change in pulse-wave amplitude and frequency does not uniformly alter footward force. Hamilton's[11] interpretation of the coarctation pattern as artifact and lack of pulse-wave reflection, therefore, seems erroneous.

Systolic wave form and the ratio of headward to footward flow remain constant throughout life, though aortic length increases enormously. The ballistic abnormality in coarctation is the same in children and adults, and in high as well as low aortic obstruction. It may be produced without altering aortic length, by changing the time course of central flow with a Hufnagel valve, and it disappears spontaneously with hemodynamic adaptation to the prosthesis.[8] Thus, the coarctation phenomenon is absent when the aorta is short but ejection normal, and may occur at any aortic length if flow is impeded.

In aortic obstructive syndromes, systolic input to the proximal segment exceeds runoff, and the distended "windkessel" maintains a high-pressure gradient across the defect well into diastole.[16] This capacitative effect delays and decreases blood deceleration in the collaterals and distal segment, thus disturbing the balance of forces responsible for normal wave form. In addition, the

ballistic effects of retrograde acceleration are minimized in the distal but not the proximal segment, thus generating a headward force prior to valve closure. The above formulation substantialy supports and elaborates Nickerson's[9] view of the mechanism of the coarctation phenomenon.

The importance of the standing wave was thoroughly analyzed by Hamilton, Dow, and Remington[11] in 1945. Despite instrumental artifact, they attributed ballistic diastole chiefly to mass movements of blood with the standing wave. Their conclusion is confirmed by the above experiments in which body distortion is minimized by improved ballistocardiograph design. Ballistic vibrations varied with change in resonator pressure, volume, elasticity, length, and coupling in cadaver and live subject as well as in model, and disappeared when resonance was abolished. Studies of limbless subjects supports Hamilton's contention that the arch vessels, iliacs, and femorals are integral parts of the systemic resonator.[12] Though diastolic vibrations originating in the pulmonary artery are normally unimportant ballistocardiographically, they may compare with the shock of aortic valve closure in patients with pulmonary hypertension and/or increased pulmonary blood flow.

The effect of the standing wave on systolic forces has not received sufficient attention. Assume the pulse wave velocity to be 5 M. per second, systolic flow velocity 100 cm. per second, the duration of ejection 0.22 second, and the reflection site to be at the level of the popliteal arteries.[12] Reflection will occur approximately 0.15 second after the aortic valves open, and the ejected "bolus" of blood will meet the returning pulse wave at the iliacs immediately before aortic valve closure. Clearly, with vasoconstriction and/or bradycardia late systolic forces may be distorted by the standing wave even in normal subjects. As demonstrated in the extreme case of the legless man, this is particularly likely in people of short stature. Though the peripheral circulation does not contribute forces, changes in vasomotor tone probably vary pulse wave velocity and the morphology of the end-systolic ballistic deflections.

SUMMARY

1. The end-systolic ballistic deflection is dependent upon deceleration of the arterial column during reduced ejection and represents a balance between headward and footward force vectors. Aortic obstruction attenuates footward force by disturbing this balance. Pulse wave reflection may modulate end-systolic force but is not essential to its genesis.

2. The initial diastolic vibrations are relatcd to the magnitude and rate of change of force with aortic valve closure. The pulmonary valve contributes only under conditions of hypertension or increased flow in the lesser circuit.

3. Vibrations subsequent to valve closure vary with aortic pressure, volume, elasticity, length, and coupling and disappear when arterial resonance is abolished. The aortic standing wave therefore seems responsible for their production. Study of limbless subjects indicates that the arch vessels, iliacs, and femorals are part of the resonator in which the standing wave oscillates.

4. Venous blood flow and ventricular relaxation do not contribute to the diastolic complex, and cardiac filling generates small vibrations unless venous return is augmented or ventricular expansion is abnormally limited.

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INFLUENCE OF A HOT AND HUMID ENVIRONMENT UPON CARDIAC OUTPUT AND WORK IN NORMAL MAN AND IN PATIENTS WITH CHRONIC CONGESTIVE HEART FAILURE AT REST

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CARDIAC output and work have been shown to be increased, for normal man at least, by a hot environment.[1-8] In experiments performed several years ago, a hot and humid environment precipitated acute left ventricular congestive heart failure in patients with mild congestive failure and in patients with cardiac compensation who were receiving therapy.[9-12] The indirect manifestations of the control subjects and the subjects with cardiac disease, as a result of the hot and humid environment, were compatible with an increase in cardiac output and work, although no direct measurements of cardiac output had been made previously. The present report concerns measurements of cardiac output, by the direct Fick method, in control subjects and subjects with chronic congestive heart failure, while the subjects rested in bed, first in a comfortable environment and then in a hot and humid one. With the use of certain necessary assumptions, time-course curves of accumulated work, volume-pressure, and tension in the cardiac wall have been constructed in order to provide a better impression of the magnitude of the changes.

MATERIALS AND METHODS

Seven subjects were studied, 3 of whom were control subjects without cardiovascular disease and 4 of whom were patients with chronic congestive heart failure. Their clinical data are summarized in Table I. The subjects with chronic congestive heart failure were carefully selected on the basis of ability to tolerate the hot and humid environment despite mild to moderate heart failure, functional Classes 2 to 3. All were under active conventional type of therapy, including digitalization, in the Charity Hospital.

The subjects were studied at least 3 hours postprandially, having had a light breakfast at about 7:30 A.M. They rested in a comfortable hospital-type bed in a comfortable, air-controlled, room atmosphere (73°F., 60 per cent relative humidity), after which cardiac output and other measurements were obtained (Table II). The room atmosphere was then made hot and humid (111°F.,

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TABLE I. CLINICAL DATA

SUBJECT NUMBER	AGE (YEARS)	SEX	COLOR	HEIGHT (INCHES)	WEIGHT (POUNDS)	CLINICAL DIAGNOSIS*	TREATMENT
				Control Series			
1	28	M	C	68.25	145.0	Duodenal ulcer, hematemesis. ECG normal	
2	51	M	C	65.75	150.0	Peptic ulcer? Gastrointestinal malignancy? Carcinoma large intestine? ECG normal. Intermittent pains both upper abdominal quadrants	
3	36	M	C	68.00	162.0	Bleeding peptic ulcer, hematemesis, and melena	
Mean	38			67.33	152.3		
				Congestive Heart Failure Series (clinically compensated)			
1	49	M	C	68.75	108.0	LVH, myocardial ischemia, RHD vs. SHD with probable aortic stenosis, relative mitral stenosis. Edema of feet. Regitine test negative	Digitalis
2	48	F	C	66.50	230.0	Hypertension, mild failure; upper gastrointestinal distress and occasional hematemesis. Slight dyspnea and edema. Acute nephritis 25 years ago	Digitalis, Raudixin
3	55	F	C	61.25	164.5	Mild failure, compensated with digitalis; diabetes 7 to 8 years. Edema of feet. Two right toes amputated	Salyrgan, digitalis, insulin
4	57	F	C	64.00	206.0	HCVD, obesity, enlarged heart, edema right leg, occasional dizziness on changing position	Was on Ansolysen† but was incapable of following instructions. Ansolysen omitted during course of these studies
Mean	52			65.12	177.1		

*LVH—Left ventricular hypertrophy, RHD—Rheumatic heart disease, SHD—Syphilitic heart disease, HCVD—Hypertensive cardiovascular disease.
†Registered trademark.

TABLE II. ARTERIAL BLOOD PRESSURE AND RIGHT VENTRICULAR PRESSURE

SUBJECT NUMBER	ARTERIAL BLOOD PRESSURE				RIGHT VENTRICULAR PRESSURE				RIGHT VENTRICULAR RATE		PRESSURE			
	SYSTOLIC (MM. Hg)		DIASTOLIC (MM. Hg)		SYSTOLIC (MM. Hg)		DIASTOLIC (MM. Hg)				RIGHT VENTRICLE (CM. H_2O)		RIGHT ATRIUM (CM. H_2O)	
	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT
Control Series														
1	118	128	74	34	17	38	5	11	72	100	17.3	16.5	10.0	11.5
2	118	130	74	70	25	33	6	8	62	80	18.5	20.0	8.5	10.0
3	144	174	70	68	26	42	3.4	8	85	110	22.0	21.0	10.0	8.0
Mean	127	144	73	57	23	38	4.8	9	73	97	19.3	19.2	9.5	9.8
Congestive Heart Failure Series (clinically compensated)														
1	168	160	110	120	56	94	11.2	13.5	88	96	29.0	——	——	——
2	220	190	130	130	24	72	7.1	24.0	54	75	——	——	——	——
3	168	132	90	76	34	52	13.0	20.0	94	100	15.5	18.8	5.6	9.0
4	174	232	86	128	41	58	8.8	11.0	75	130	29.5	43.0	5.0	16.5
Mean	183	179	104	114	39	69	10.5	17.1	78	100	24.7	30.9	5.3	12.7

86 per cent relative humidity), rather slowly over a period of about 1 hour, since it was not known how well the subjects with congestive failure would tolerate the environment and manipulations. The measurements were recorded again.

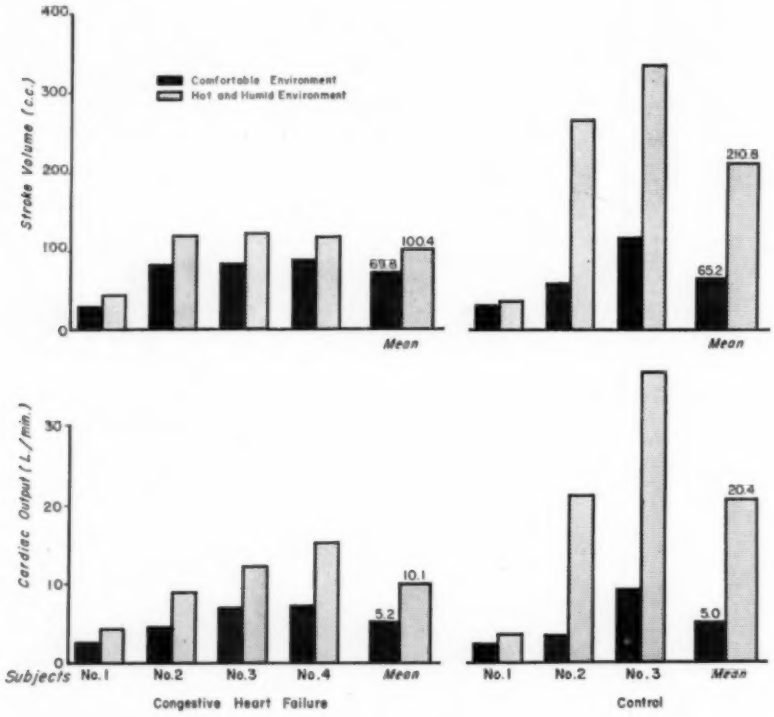

Fig. 1.—Influence of hot and humid environment on cardiac output and stroke volume in 3 control subjects and in 4 patients with congestive heart failure. No correction was made in this study for surface area, because the formula for calculating surface area from body weight and height includes an unknown, but sizable, error. Such a conversion was not necessary for this study but may be obtained from use of Table I.

Output of the right and left ventricles was measured by the direct Fick principle, with the use of the conventional, present-day methods of cardiac catheterization.[13,14] The pressure in the right ventricle was recorded continuously with a strain gauge and string-type of electrocardiograph galvonometer.* Mean pressure in the veins through which the cardiac catheter passed on its way to the heart was measured with a water manometer. The blood gases were determined by the method of Roughton and Scholander,[15] and the oxygen in the expired air was measured with the use of the Beckman oxygen analyzer (Model No. 2).

All subjects were repeatedly examined clinically during the experiments, and a record was made of the pulse and respiratory rates, blood pressure, general appearance, and subjective reactions to the environment, which were evaluated by questioning and degree of sweating. The electrocardiogram, as well as direct measurements of cardiac output, right intra-atrial and intraventricular pressures, were also recorded. Final recordings were obtained when it was

*Simplitrol, Cambridge Instrument Co., New York.

considered inadvisable to continue the exposure of the subject more than an additional 15 minutes.

RESULTS

Results are summarized by Tables II and III, and Figs. 1 to 7.

Cardiac Output and Stroke Volume.—Cardiac output and stroke volume increased in every subject at rest, upon exposure to the hot and humid enviroment (Fig. 1). The increase was over threefold in the control subjects, whereas it was not quite twofold in the subjects with congestive heart failure. Control

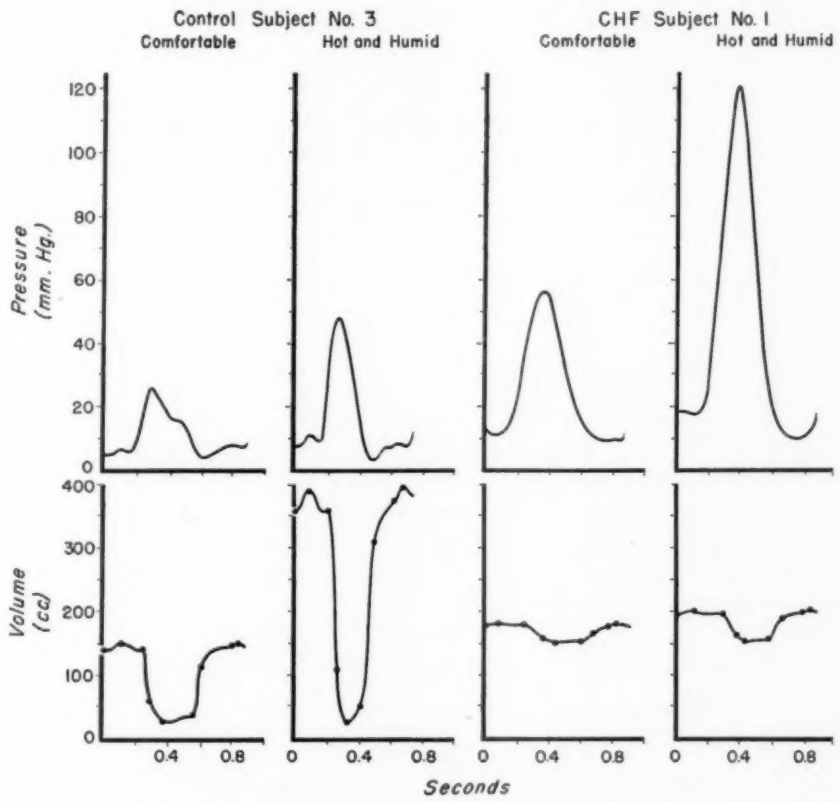

Fig. 2.—Influence of hot and humid environment on simultaneous pressure and volume of the right ventricle for a control subject (No. 3) and a subject with chronic congestive failure (No. 1). (See text for details of assumptions.) Considerably higher pressure was developed by the myocardium of the right ventricle of the subject with congestive failure than by that of the control subject, with ejection of much less blood per cardiac stroke, an interesting and not unexpected finding for congestive failure.

Subject No. 1 had a relatively small increase in cardiac output. This may have been the result of effects of acclimatization, since this man worked in a boiler room where the temperature was even hotter than it was in these experimental conditions. The mean increase in cardiac output for the control subjects was from 5 to 20 L. per minute and from 5 to 10 L. per minute for the subjects with heart failure. Individual variations are shown in Fig. 1.

Volume-Pressure Time-Course Curves.—For more extensive evaluation of the limited data, they were charted as various types of volume-pressure time-

TABLE III. RESPIRATORY PARAMETERS

SUBJECT NUMBER	VENTILATION RATE (L./MIN.)		TIDAL AIR (C.C.)		O_2 CONSUMPTION (C.C./MIN.)		A-V DIFFERENCE (C.C./100 C.C. BLOOD)		O_2 CONTENT ARTERIAL (C.C./100 C.C. BLOOD)		O_2 CONTENT VENOUS (C.C./100 C.C. BLOOD)		RESPIRATION (TIMES/MIN.)	
	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT
Control Series														
1	4.48	8.08	266.0	680.0	246.3	447.3	11.3	12.8	18.25	18.67	6.89	5.89	17	12
2	3.44	13.08	314.5	550.2	118.0	738.0	3.7	3.6	16.83	17.10	13.12	13.49	11	24
3	6.20	16.00	223.1	537.9	283.0	803.0	2.93	2.19	14.05	13.77	11.01	11.86	28	30
Mean	4.71	12.38	267.9	589.4	215.8	662.7	6.0	6.2	16.38	16.51	10.34	10.41	19	22
Congestive Heart Failure Series (clinically compensated)														
1	8.35	10.4	279.5	307.4	198.0	292.0	8.45	7.2	17.34	16.52	9.76	9.91	30	34
2	7.38	11.4	370.8	286.6	207.0	373.0	4.9	4.2	—	—	—	—	20	40
3	7.28	13.0	236.3	326.8	264.0	430.0	3.8	3.6	12.77	12.59	9.26	9.44	31	40
4	6.60	12.7	415.8	492.4	311.7	599.8	4.4	4.0	17.50	17.60	13.30	13.90	16	26
Mean	7.40	11.9	325.6	353.3	245.2	423.7	5.4	4.8	15.87	15.57	10.77	11.08	24	35

course curves for a representative control subject and a subject with chronic congestive heart failure, as described previously[16] (Figs. 2 to 5). This, however, necessitated certain assumptions. The time-course curves of right ventricular pressure were recorded directly, whereas the pressure curves for the left ventricle and the time-course curves of volume for both ventricles were

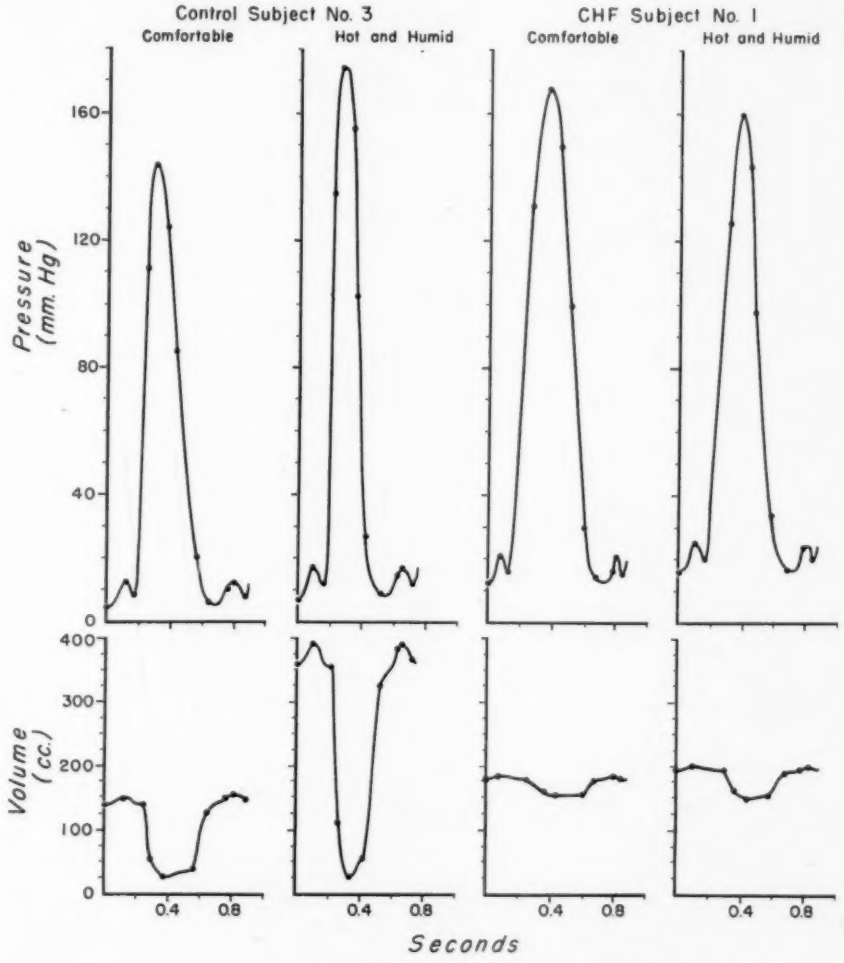

Fig. 3.—Influence of hot and humid environment on time courses of pressure and volume of the left ventricle for the same cardiac cycle and same subjects shown in Fig. 2. Although a proportionately higher pressure was developed by the myocardium of the left ventricle to eject a given volume of blood in the patient with chronic congestive failure than in the normal subject, this difference was not as great as for the right ventricle (consult Fig. 2).

assumed to vary with time in the pattern described by Wiggers,[5] the maximal and minimal levels in pressure attained in the curves of the left ventricles being those recorded by the sphygmomanometer, and the maximal volume ejected by both ventricles being the stroke volume measured in these studies. The end systolic volume used for the control subjects was 25 c.c., whereas that for the subjects with congestive failure was 150 c.c., both assumed but reasonable values.

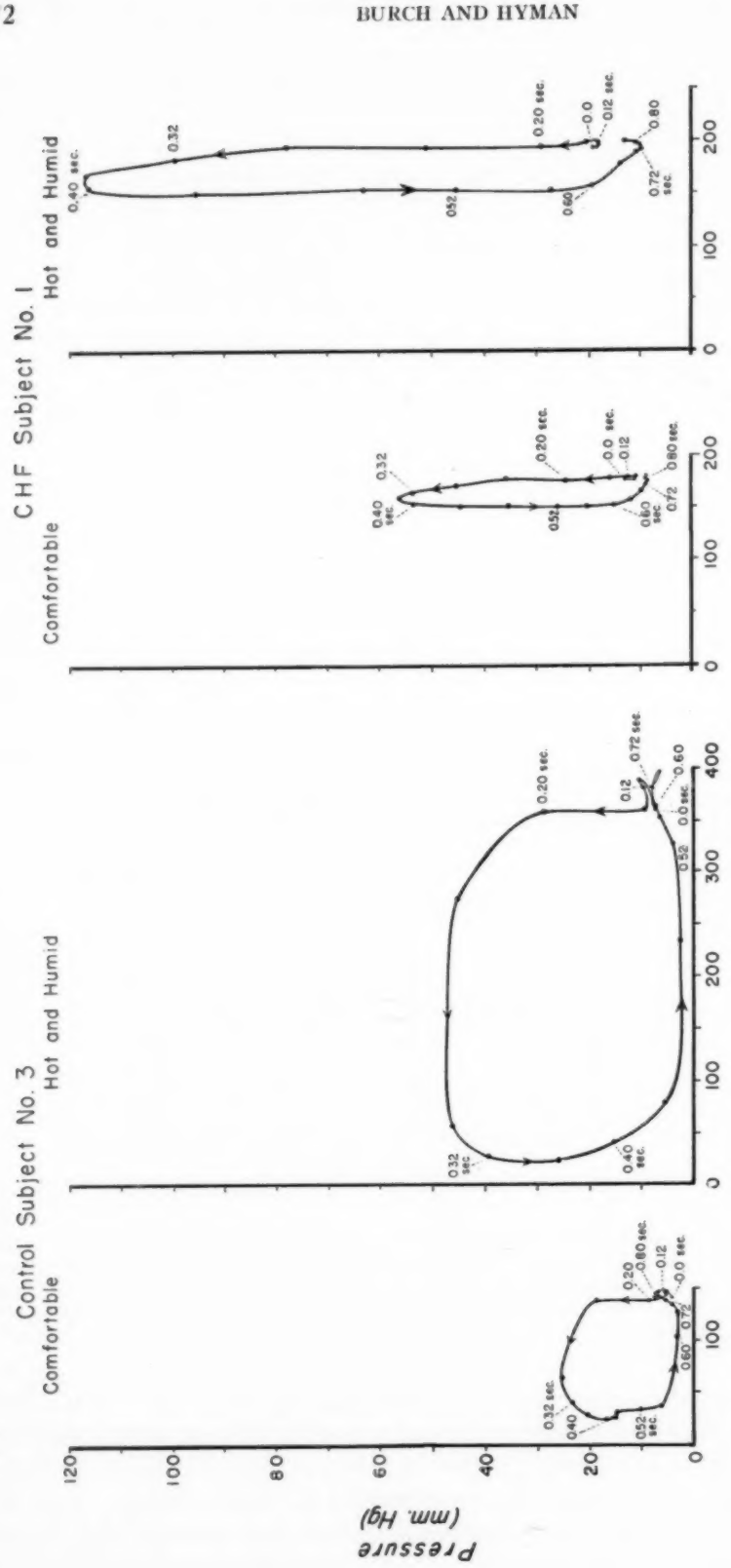

Fig. 4.—Influence of hot and humid environment on volume-pressure-time "loops" of the right ventricle for a control subject and a subject with chronic congestive heart failure. The more "vertical" loops for the subject with failure was characteristic for both ventricles (Fig. 4) of all such subjects studied. This vertical configuration of the loops is further evidence of the development of a relatively high pressure by the myocardium in order to eject a relatively small volume of blood per stroke. The area under these loops is an index of the work produced by the myocardium for that cardiac cycle.

If the assumptions employed do not deviate too greatly from the actual physiologic state, then the configurations of the curves shown in Figs. 2 through 5 for the control subject differ from those for the subject with congestive heart failure. The shapes of the two groups of curves were found to be consistently different, those for subjects with congestive failure being more "vertical" in shape. A study of these illustrations will reveal aspects of the respective physiologic states.

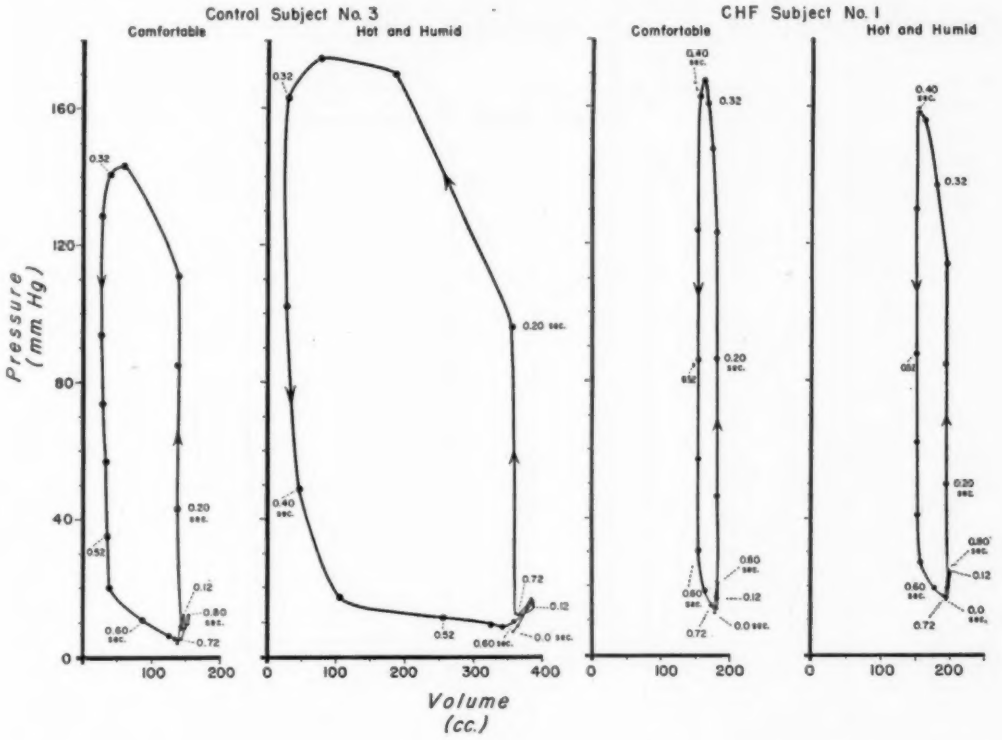

Fig. 5.—Influence of hot and humid environment on volume-pressure-time "loops" of the left ventricle for the same control subject and for the subject with chronic congestive heart failure shown in the preceding illustrations. Consult legend of Fig. 4.

Time-Course Curves of Accumulated Mechanical Work.—Since the work of the ventricle is expressed as

$$W = \int PdV,$$

then from the curves of Figs. 2 through 5 it is possible to obtain the time-course curves of accumulated work, as shown in Fig. 6, for 2 representative subjects with and without congestive failure. The heart of the control subject worked relatively more than did that of the subject with failure at rest in a comfortable environment. When the environment was made hot and humid (Fig. 6), the cardiac work increased in all subjects but was much more pronounced in the control subjects.

The first and second derivatives of these work curves resulted in time-course curves of power and acceleration in power. For the sake of brevity,

these have been omitted, but they can readily be derived by inspection of the work curves.

Time Course of Tension of the Wall of the Ventricles.—The time-course curves of tension of the wall of the ventricles, shown in Fig. 7, were obtained as described previously[16,17] and were based upon the expression:

$$T = \frac{RP}{2},$$

where R is the radius of a spherical-shaped ventricle and P is the intraventri-

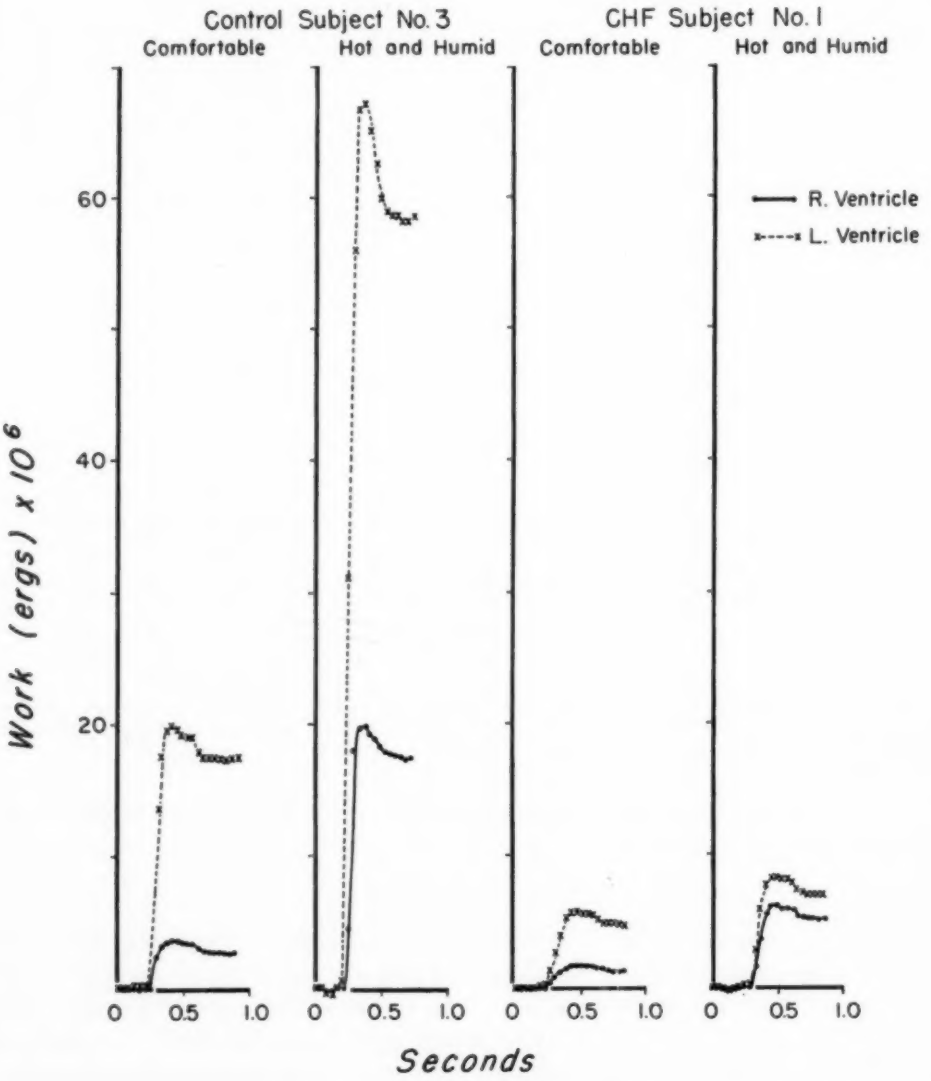

Fig. 6.—Influence of hot and humid environment on time course of accumulated work for the right and left ventricles for the same cardiac cycle and same subjects shown in the previous illustrations. It is evident that, although the subject with failure was stimulated by the humid heat so that the work of his two ventricles was increased, he was not able to do so nearly to the same extent as the normal control subject under the same type of stimulus (an important difference for the decompensated heart).

cular pressure. These curves represent the tension in dynes/cm. on the wall of the ventricles during the cardiac cycle. The assumption that the ventricles are spherical is obviously erroneous but of value for these discussions. The volume and pressure variations used in these illustrations were the same as those employed in the other illustrations of this report. Fig. 7 shows the time

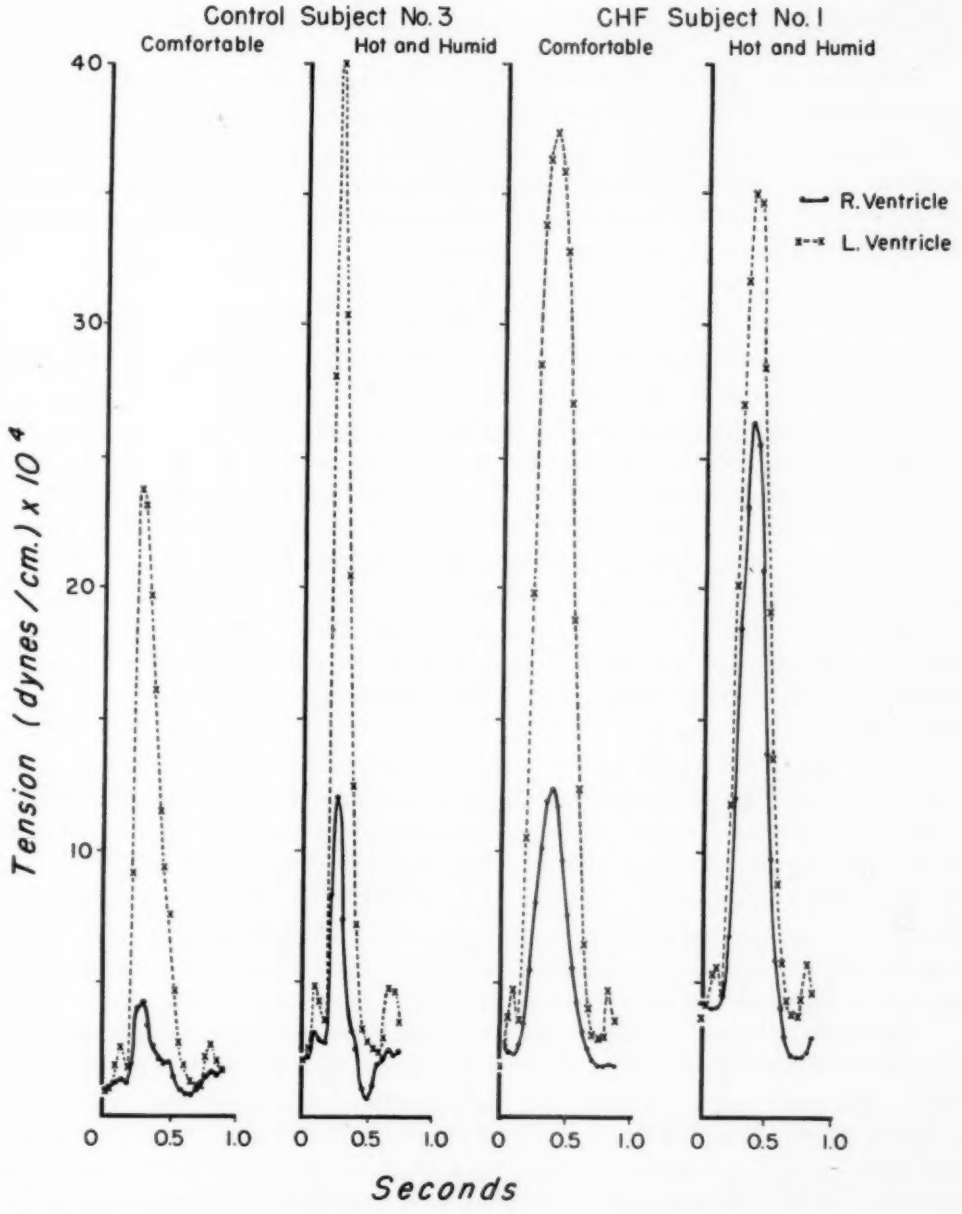

Fig. 7.—Influence of hot and humid environment on time course of tension developed in the walls of the right and left ventricles of the same control subject and of the subject with chronic congestive heart failure, as in the previous illustrations. In the subject with failure, relatively more tension developed to eject less blood per stroke than in the control subject.

course of tension in the ventricular walls to be greater at rest in the subject with congestive heart failure and to have increased in both subjects studied, but to a greater degree in the subject with chronic congestive heart failure than in the control subject except for the left ventricle. Because of cardiac dilatation and greater residual or end-diastolic volume in congestive heart failure, tension in the wall of the ventricles tends to be greater and the ventricles tend to be less efficient, from the point of view of tension, than in a normal-sized heart.

Miscellaneous Results.—Tables II and III summarize some of the physiologic influences of the hot and humid environment, including such data as the A-V oxygen difference, pulse rate, respiratory rate, and degree of oxygen extraction. As expected, the more distal the vein was from the heart, the greater was the venous pressure, with a more noticeable rise in pressure as the catheter was withdrawn from the veins of the thorax.

DISCUSSION

These experiments show that a hot and humid environment will increase cardiac output, stroke volume of the ventricle, mechanical and physiologic cardiac work, and tension upon the walls of the ventricles. The detailed mechanisms by which the increase in cardiac work occurs are unknown but are related to thermal regulation. Thus, a subject lying supine in bed can increase his cardiac work without exercise and without movement. This is not only convenient and advantageous for complex experimental procedures but is also useful in revealing differences in "effective" exertion, from the cardiovascular point of view, for different environmental conditions. For example, relatively mild exercise in a hot and humid environment would be expected, from these studies, to produce more cardiac work than strenuous exercise in a cool and dry environment.

These experiments demonstrate further the need for considering environment and advice to patients about their activity during cardiac therapy.[18] It must be realized, of course, that these experiments were acute and were thus free from the compensating influences of acclimatizing accommodations. Furthermore, the temperature and relative humidity in these experiments were relatively high and would be encountered rarely. As noted elsewhere,[18] a balmy climate, with adequate consideration of physical exertion and air conditioning, appears to be most conducive to cardiac rest.

Because of the stress of the hot and humid environment and the added risk of cardiac catheterization, it was considered advisable to study only a few subjects. The subjects withstood the experiments remarkably well, but there is a need to study this problem more extensively under greater ranges of temperature and humidity, under various types and degrees of mental and physical activity, and for various types and degrees of cardiovascular disturbances. The nature and influence of acclimatization upon cardiac work also require investigation.

The analyses and curves presented in this report (Figs. 2 to 7) provide a different approach to the visualization of the data and emphasize the differences

TABLE IV. CARDIAC WORK

SUBJECT NUMBER	CARDIAC OUTPUT (L./MIN.)		STROKE VOLUME (C.C.)		SYSTEMIC RESISTANCE (DYNE-SEC./CM.^{5})		HEAT PRODUCED (CAL./HR.)		BODY TEMPERATURE CHEST °F.		BODY TEMPERATURE RECTUM °F.	
	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT	COMF.	HOT
Control Series												
1	2.2	3.5	30.6	35.0	3199	1668	71.5	129.8	91.2	97.9	93.6	97.2
2	3.2	20.5	51.6	256.2	2199	359	34.3	214.2	91.6	95.4	93.9	95.4
3	9.6	36.6	112.9	332.7	825	247	82.2	231.1	92.8	99.5	96.1	98.6
Mean	5.0	20.2	65.0	208.0	2074	758	62.7	192.4	91.9	97.6	94.5	97.1
Congestive Heart Failure Series (clinically compensated)												
1	2.34	4.1	26.6	43.8	4477	2574	57.5	84.8	93.6	97.2	——	——
2	4.2	8.9	77.8	118.7	3180	1365	60.1	108.3	84.2	94.0	——	——
3	6.9	11.9	73.4	119.0	1403	645	76.6	124.8	92.2	96.8	94.3	95.9
4	7.1	15.0	95.0	115.0	1374	917	90.5	174.1	92.5	97.2	94.8	96.3
Mean	5.1	10.0	68.2	99.1	2609	1375	71.2	123.0	90.6	96.3	94.6	96.1

between the control subjects and those with congestive failure. The configurations of the pressure-volume time-course "loops" were particularly different; the "vertical" type of loops in the subjects with congestive heart failure would be of diagnostic and clinical value if they could be readily obtained in intact man and proved to be characteristic of poor cardiac reserve. Surely, there is a need to develop a method for simple automatic recording of such loops in intact man. The continuous curves shown in this report present quantitative data crudely, because the assumptions made to obtain them, although obviously erroneous, were of sufficient accuracy for effective and provocative presentation of the data and concepts.

As noted from Table IV and Fig. 1, the cardiac output and stroke volume in some subjects were fairly large. This may be due in part to error intrinsic in the Fick procedure, which is even more likely in this group of experiments because of the small A-V oxygen differences encountered. However, magnitudes of this sort have been obtained previously by others.[19-22]

Differences were noted between the influence of hot and humid environments upon the circulation in these experiments and the effect of exercise reported by others.[6-8] Although these differences are evident in the accompanying tables and the reports of others, certain ones should be mentioned. For example, the A-V oxygen differences were increased by exercise but remained essentially unaltered in the control subjects and were reduced slightly in the patients with congestive heart failure by the hot and humid environment. Oxygen consumption was increased more by exercise than by the hot and humid environments. Cardiac rate was increased much more per unit elevation in cardiac output by the hot and humid environment than by exercise, as reported by others. Thus, stroke volume seems to be increased more by hot and humid environments than by exercise, but one cannot be certain about this, because of difficulties in evaluating properly the relative degrees of influence of exercise and of hot and humid environments, and because the studies were performed in different laboratories where other variables may have been significant. It does appear from clinical and personal experience, as well as plethysmographic studies, that exercise increases cardiac output in large part by increasing cardiac rate. A full, bounding, and relatively slow pulse with large volume pulse waves in the digits[23] has been noted for man at rest in a hot and humid environment. Exertion under such environmental conditions would be expected to add the cardiovascular and other physiologic responses to those produced by the hot and humid environments alone.[24,25] The mechanisms and differences by which cardiac output is increased by a hot and humid environment and by exercise need careful study. Although concepts concerning these mechanisms exist, any comments concerning them would only be conjectural or would consist of a review of the literature and would, therefore, contribute little to this report.

Other types of curves[16] obtained from the pressure and volume curves were omitted to conserve space, but they may be obtained relatively easily from Figs. 2 through 7.

SUMMARY

Acute experiments on normal subjects and patients with chronic congestive heart failure, at rest, revealed that a hot and humid environment produced a considerable increase in cardiac work, cardiac output, and stroke volume in the normal subjects and definite, but less, increase in the patients with congestive heart failure. The increase in cardiac work and output occurred more as a result of a larger stroke volume than greater cardiac rate, in comparison with effects of exercise reported by others.

Other cardiovascular and respiratory phenomena were also observed. There is evidence from these results and the cardiac response that a hot and humid environment produced a considerable stress upon the heart and circulation. The possible therapeutic implications in subjects with cardiovascular disease and other illnesses have been discussed.

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HEMODYNAMICS IN ATRIAL FLUTTER WITH SPONTANEOUS REVERSION TO NORMAL SINUS RHYTHM

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THE hemodynamic effects of abnormal cardiac rhythms have been difficult to evaluate in man. The problem of isolating the effects of a change in the cardiac pacemaker from the effects of alterations in cardiac function induced by therapy has been almost insurmountable. In the literature there are no available comparisons of over-all hemodynamics during arrhythmias and during normal sinus rhythm in which other variables or appreciable time lag did not intervene during the course of the investigation.

Fortuitously, we had the opportunity to measure circulatory dynamics under closely controlled conditions in a patient who, during the course of a cardiac catheterization, developed atrial flutter and spontaneously reverted to normal rhythm. Since the opportunity to make such observations occurs rarely, we are reporting them at the present time.

CASE REPORT

A 31-year-old housewife had undergone a successful mitral valvuloplasty 29 months previously. Although symptomatic improvement followed the operation, she continued to take digitoxin, 0.1 mg. daily, as she had for three and one-half years. During the month prior to readmission she had noted some dyspnea and cough associated with a series of respiratory infections. The possibility of the mitral valve having resealed was considered and the patient was readmitted to the New York Hospital on Oct. 28, 1955, for re-evaluation of her cardiac status. Physical examination revealed a well-developed, white woman with a blood pressure of 115/70 mm. Hg. A thoracotomy scar was present on the left chest. The heart was slightly enlarged to the left; the rhythm was regular with a rate of 88. The first mitral sound was snapping; the second pulmonic sound was accentuated, and an apical presystolic thrill and rumbling murmur were present. There were no signs of cardiac failure. Complete blood count, urinalysis, liver function tests, and electrolytic studies were normal. An electrocardiogram revealed normal sinus rhythm (NSR), incomplete right bundle branch block, with a rsR′ pattern (intrinsicoid deflection delayed to 0.05 second) in V_1. In comparison to the preoperative record, significant regression of the alterations associated with right ventricular hypertrophy had occurred. No significant change had occurred in the left atrial and pulmonary arterial enlargement noted preoperatively in roentgenograms and fluoroscopy of the heart.

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Cardiac catheterization was performed on Nov. 3, 1955. Early during the procedure, while the catheter was being manipulated in the right atrium, the rhythm changed from normal sinus at a rate of 100 to atrial flutter, with 3:1 and 4:1 atrioventricular block, an atrial rate of 300 and a ventricular rate that continued at 100. The patient was neither aware nor informed of the onset or persistence of the arrhythmia. Since there were no symptoms referable to the flutter, the procedure was not interrupted and measurements were made during rest and exercise. Within a few minutes after completion of the exercise, the atrial rate increased to 430 (flutter-fibrillation). Atrial fibrillation ensued, persisted for a minute, and was followed by reversion to normal sinus rhythm. The ventricular rate remained at 100. Within one hour after reversion, measurements were again made at rest. Because of the length of the procedure exercise was not repeated.

The technique of cardiac catheterization and the analytic methods employed were as previously described.[1]

RESULTS

The cardiac output was normal during flutter and decreased slightly after reversion to NSR (Table I). The lower consumption of oxygen during NSR than during flutter accounted entirely for the decrease in cardiac output, since the arteriovenous oxygen difference did not change. The respiratory quotient (an index of the "steady state"[2]) was identical in both periods.

TABLE I. DATA PERTAINING TO RESPIRATION AND CARDIAC OUTPUT

	ATRIAL FLUTTER	NSR
Ventilation (L./min./M.²)	4.23	3.87
Respiratory quotient	0.76	0.76
Oxygen consumption (c.c./min./M.²)	153	131
Arteriovenous oxygen difference (vol. %)	4.63	4.61
Cardiac output (L./min./M.²)	3.30	2.84
Ventricular rate	100	100
Stroke volume (c.c.)	48	41

The pulmonary "capillary" ("PC"), pulmonary arterial, and right ventricular pressures, and the pulmonary vascular resistance (PVR) were moderately elevated (Table II), but considerably lower than they had been preoperatively.

TABLE II. PRESSURES IN MILLIMETERS OF MERCURY OBTAINED DURING CARDIAC CATHETERIZATION

	ATRIAL FLUTTER	NSR
Pulmonary "capillary" mean	21	20
Pulmonary artery		
systolic/diastolic	47/25	48/27
mean	38	39
Right ventricle	47/2	48/2

Repeated measurements of resting pressures throughout the procedure revealed no consistent change in their levels with variation in rhythm. During

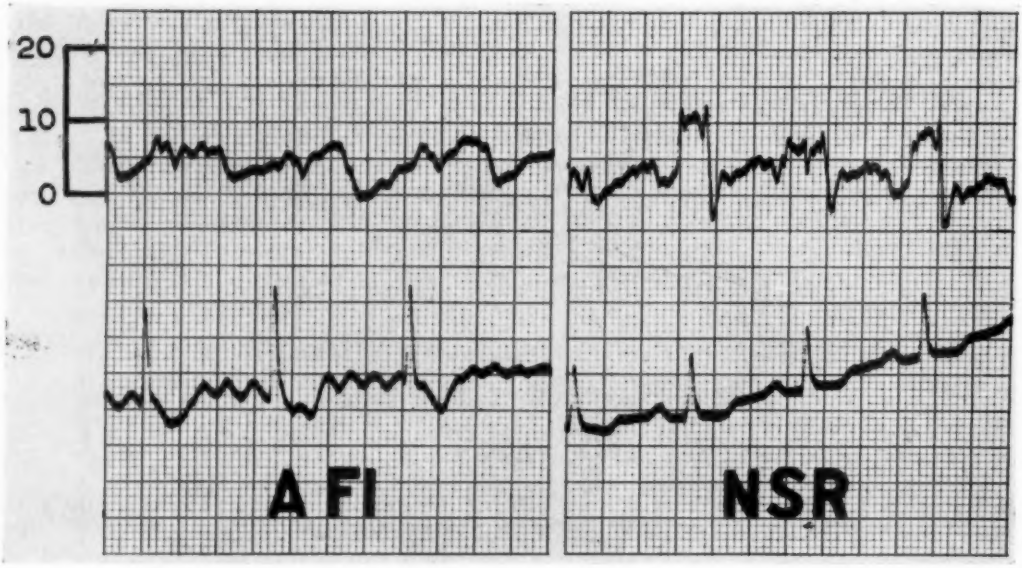

Fig. 1.—Right atrial pressure curves and simultaneously recorded ECG Lead II during flutter fibrillation (*AFl*) and normal sinus rhythm (*NSR*). In *AFl*, atrial systole is absent. There is an increase in pressure that persists throughout ventricular systole and a "peak-dome" pattern characteristic of tricuspid insufficiency. In *NSR* evidence of tricuspid insufficiency is absent; atrial contraction is followed by a sharp drop in pressure during ventricular systole. (Scale to left in this and in subsequent figures is in mm. Hg.)

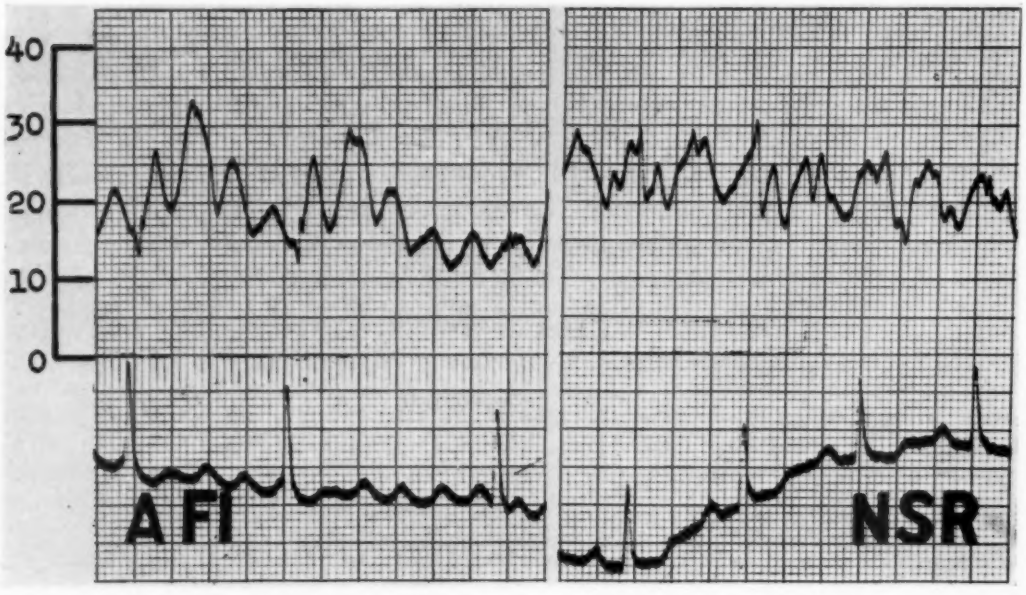

Fig. 2.—Pulmonary "capillary" pressure tracings and simultaneously recorded ECG Lead II during flutter (*AFl*) and normal sinus rhythm (*NSR*). In *AFl*, the increase of pressure that is sustained throughout ventricular systole is evidence of mitral insufficiency. During *NSR* the pattern of the tracing is normal; the pressure falls with the onset of ventricular systole.

flutter, however, transient increases of ventricular rate from 100 to 110 were associated with a corresponding 3 mm. increase in "PC" pressure and 4 mm. rise in mean pulmonary arterial pressure.

The configuration of the right atrial (Fig. 1) and "PC" (Fig. 2) pressure curves during flutter (flutter-fibrillation in the right atrial tracing) differed considerably from the curves recorded during NSR. During flutter there was an elevation of pressure that persisted throughout ventricular systole in both the right atrium and "PC" position. These pressure patterns were considered pathognomonic of tricuspid insufficiency[3,4] and mitral insufficiency,[5,6] respectively. In contrast, during normal sinus rhythm, a drop of pressure, which characteristically develops when the atrioventricular valves are competent,[3,6] occurred in the right atrium and "PC" position during ventricular systole.

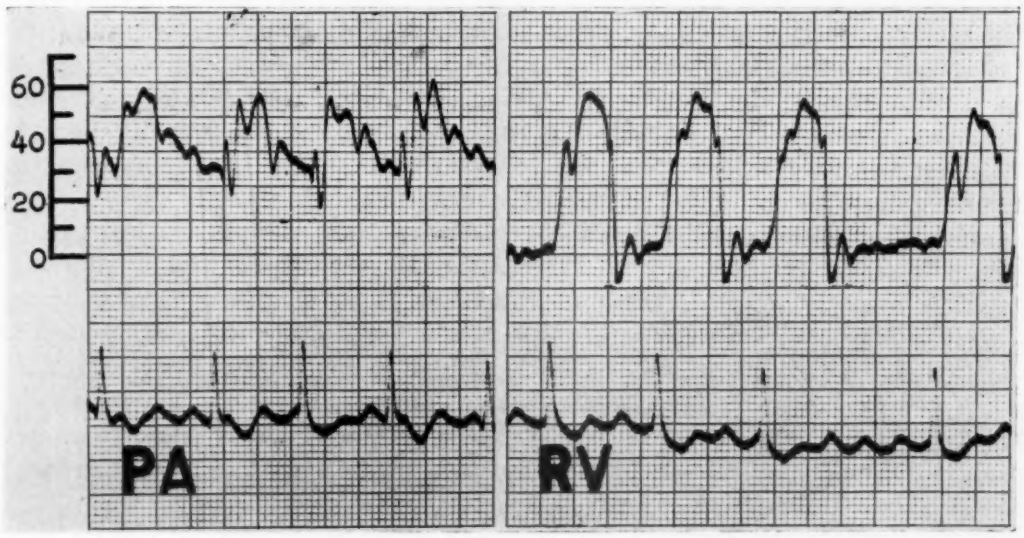

Fig. 3.—Pressure curves recorded from the pulmonary artery (*PA*) and right ventricle (*RV*) during atrial flutter with simultaneously recorded Lead II. Small atrial contraction waves are evident in both tracings during diastole.

Small atrial contraction waves related to the flutter waves in the electrocardiogram, but slightly delayed, were present in the right atrial and the "PC" pressure tracings (Fig. 2) and during diastole in the pulmonary arterial and right ventricular tracings (Fig. 3).

When exercise was performed in the flutter period, the cardiac output rose slightly to 3.5 L./min./M.^{2}; the "PC" pressure increased to 32 mm. Hg, and the pulmonary artery mean pressure to 61 mm. Hg. This was in contrast to the fall in cardiac output and the rise in pulmonary arterial pressure to above systemic levels that was observed preoperatively during exercise. Exercise was not repeated after reversion to NSR.

DISCUSSION

The inherent difficulty in determining the effect of an arrhythmia lies in the exclusion of factors, other than a shift in the pacemaker, which may influence cardiovascular function. Change in heart rate and alteration in the state of cardiac compensation, which may follow the administration of digitalis, quinidine, diuretics, and bed rest, frequently interfere with the interpretation of the data. The longer the interval between observations made during a particular rhythm and those following conversion to another rhythm in a patient under treatment, the more difficult it is to ascribe measured alterations in cardiovascular function to the change in rhythm alone. A study of atrial fibrillation[7] suffers from these defects. The conclusions arrived at in a recent report on atrial flutter[8] are also tempered, as the authors recognize, by these considerations.

By fortuitous circumstances, our study was undertaken under almost ideal conditions for evaluating the effect of atrial flutter on cardiac function. The data during flutter and NSR were obtained in the course of the same procedure. The rate remained constant; no drugs were used, and the respiratory quotient was identical during both rhythms.

Under these circumstances the cardiac output and pressure levels in the right heart chambers and pulmonary vascular bed were not significantly affected when atrial flutter was replaced by normal rhythm. The small decrease in cardiac output during NSR was related entirely to the decrease in oxygen consumption, and therefore could not be ascribed to intrinsic change in cardiac function. The decreased oxygen consumption was probably associated with lessening anxiety[9] as the procedure progressed. The maintenance of cardiac output at normal levels during atrial flutter is compatible with the evidence that atrial contraction contributes only slightly to ventricular filling at rates below 160.[10,11] Two reported cases of nodal tachycardia, a rhythm in which atrial and ventricular contractions are not in normal temporal sequence, were studied during both NSR and the arrhythmia in the course of one procedure and also showed no change in cardiac output.[12]

The appearance of mitral and tricuspid insufficiency during flutter, and the restoration of valve competency with NSR are significant in light of the demonstration by Little[13,14] that atrial contraction with a normal temporal relationship to ventricular systole is necessary to insure adequate closure of these valves, prior to the onset of ventricular contraction. If atrial contraction is not present, or if the interval between atrial and ventricular systole is abnormally short or long, regurgitation will occur, because the valves are wide open at the instant of ventricular contraction. Although atrial flutter may be associated with forceful contractions of the atria,[15] these contractions were apparently neither forceful enough nor in proper sequence with ventricular systole in our patient to effect adequate closure of the atrioventricular valves before the onset of ventricular contraction and regurgitation occurred. This mechanism may have been responsible for the development of tricuspid insufficiency in 2 patients during nodal tachycardia.[12] In patients with rheumatic heart disease and atrial fibrillation, the absence of an atrial contraction is partially responsible for the high incidence of tricuspid insufficiency.[4]

Although tricuspid insufficiency was apparent in our case, and in a case recently reported by McCord and Blount[15] (see their Fig. 4), it was not observed in 12 other cases of flutter studied by Harvey and associates.[8] However, the lack of a definite decrease in pressure with onset of ventricular systole in two of the right atrial tracings (see Figs. 1 and 4 in Reference 8) can be regarded as evidence of inadequate closure of the tricuspid valve.

Small positive pressure waves, corresponding to the flutter waves in the electrocardiogram, have been noted previously in the diastolic segments of brachial and pulmonary arterial pressure curves.[8,15] Their appearance in systemic arterial pressure curves is not readily explained. In the pulmonary artery, on the other hand, backward transmission of these waves from the left atrium is not at all unlikely, since positive pressures generated in the left atrium may be recorded from the pulmonary artery, particularly when the pulmonary vascular resistance is low. Left atrial pressure phenomena are recorded from an obstructed pulmonary artery with little difficulty.[16]

We do not believe that our data can be interpreted to indicate that atrial flutter is physiologically as satisfactory as NSR in the patient with heart disease. On the contrary, since the ventricular rate in flutter may be difficult to control, particularly during exercise,[17] this rhythm is probably disadvantageous. At rapid rates ventricular filling is impaired both by shortening of ventricular diastasis and by loss of atrial contraction, which contributes more to filling than at slow rates.[10] The general level of the cardiac output during the course of the daily activities of a patient with inadequately controlled flutter would therefore be expected to be lower than if NSR were present.

An additional disadvantage to the patient with mitral stenosis results from the increase in left atrial, pulmonary, arterial, and right ventricular pressures occurring with increase in ventricular rate in this disease.[1,18,19] In our patient, transient, spontaneous increases in rate during flutter were associated with concomitant, small increases in pulmonary vascular pressures.

The degree to which flutter contributed to the inadequate rise of cardiac output and to the increase in pressures during exercise cannot be assessed, since exercise was not repeated after reversion to NSR. The exercise ventricular rate of 140 per minute, however, was somewhat greater than would be expected with NSR and the same degree of exercise.

SUMMARY

During cardiac catheterization of a 31-year-old woman with mitral stenosis, the development of atrial flutter and subsequent spontaneous reversion to normal sinus rhythm provided an opportunity to study the hemodynamic effects of the arrhythmia under ideally controlled conditions. The ventricular rate remained constant; no cardiac drugs were administered, and the patient, who was neither aware of the arrhythmia nor had symptoms referable to it, remained in a fairly stable, steady state.

Neither cardiac output nor pressure levels in the heart and the pulmonary vascular bed were altered significantly by the atrial flutter. Evidence of mitral

and tricuspid insufficiency appeared during the arrhythmia but was not present during sinus rhythm. The valvular dysfunction was related to the current concept of the importance of normal atrial contraction to adequate closure of the atrioventricular valves.

We are grateful to Dr. Gordon Howe for referring this patient to us.

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DETERMINANTS OF THE CIRCULATORY RESPONSE TO HYPOXIA AND HYPERCAPNIA

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INTRODUCTION

FURTHER knowledge of the mechanisms by which hypoxia and hypercapnia alter the circulation would add to the understanding of many clinical problems. Though reflexes reponsible for adjusting heart rate, ventilation, and peripheral vascular tone to changes in blood O_2 and CO_2 tension have been fully described,[1-5] the separate effects of hypoxia and hypercapnia on heart muscle are less well understood. The role of direct chemoreflex modulation of ventricular contractility is unknown, and the function of epinephrine in moderate hypoxia and in hypercapnia remains controversial.[5-8] Direct cardiovascular depression as well as hemodynamic changes secondary to altered ventilation complicate the response of the intact animal.[2,9,10] In the present study we have sought to examine the direct and centrally mediated determinants of the circulation in moderate hypoxia and varying degrees of hypercapnia.

METHODS

The effect of 12 per cent O_2 and 6 per cent CO_2 on blood volume distribution was measured as change in body center of gravity. The method employs a recording teeterboard, thoracic and abdominal pneumographs, and an extremity plethysmograph as previously reported.[11-13]

Reaction force was measured with a modified Wittern ballistocardiograph, the mechanical constants of which minimize tissue distortion.[14,15] A detailed description of the apparatus and the relationship between the ultra-low-frequency ballistocardiogram and physiologic events has been presented.[16] Though motions unrelated to ejection complicate the record, a discrete systolic wave originated by central arterial flow may be identified; force as used herein refers solely to this deflection. Mean longitudinal and mean lateral or anteroposterior forces throughout a respiratory cycle were used to calculate a frontal or sagittal plane force vector. The electrocardiogram, arterial pressure, or both were recorded for reference throughout every experiment.

Epinephrine was assayed with the denervation-sensitized nictitating membrane of cats.[17] The preparation is about equally responsive to epinephrine and norepinephrine. Fresh dilutions of 1 c.c. ampules of 1:1,000 epinephrine hydrochloride were used for calibration, and the experimental results were expressed in micrograms of epinephrine. The method detects a minimal concentration of 0.1 to 0.2 mcg.

Ventilation was measured through a mask equipped with a check valve, the inspiratory side of which opened to room air or test mixture, the expiratory side to a low resistance wet-test gas meter.

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The effects of 10 per cent O_2 and 6 per cent CO_2 were observed in 10 healthy mongrel dogs anesthetized with pentobarbital, 27 mg. per kilogram body weight, curarized with 3 c.c. succinylcholine chloride and maintained on constant ventilation with a Seeler resuscitator.[18*] When adjusted to cycle about a mean pressure of 0 to plus 2 mm. Hg, dogs could be ventilated for over an hour without significant change in ballistocardiogram or arterial pressure. Five animals were restudied 10 days later under hexamethonium or dibenamine, and 20 days later after vagotomy, carotid sinus denervation and vagotomy, adrenalectomy, or decapitation. A separate group of 6 dogs was used to study the effects of 10 to 30 per cent CO_2. Gas mixture employed included: 10 per cent O_2 in 90 per cent N_2, 6 per cent CO_2 in 94 per cent O_2, 10 per cent CO_2 in 90 per cent O_2, 15 per cent CO_2 in 85 per cent O_2, 20 per cent CO_2 in 80 per cenr O_2, and 30 per cent CO_2 in 70 per cent O_2.

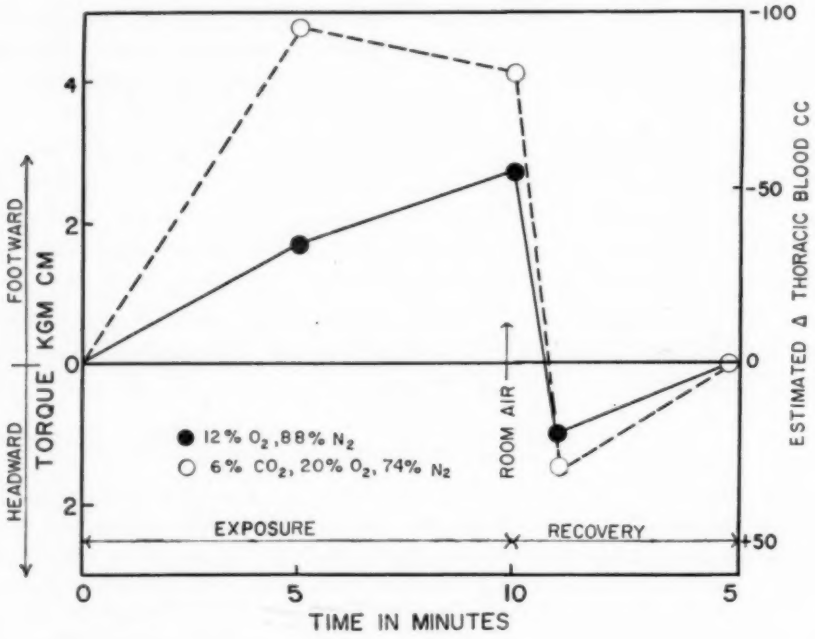

Fig. 1.—Mean change in blood volume distribution among 12 normal human beings breathing 10 per cent O_2 and 6 per cent CO_2.

RESULTS

A. *Effect on Blood Volume Distribution.*—Fig. 1 represents the mean center of gravity change effected by 12 per cent O_2 and 6 per cent CO_2 in 12 normal subjects. The response was consistent in each: a slight shift of center of gravity footward, no change in extremity volume, and slight increase in thoracic midposition under hypoxia, but not with hypercapnia. Note that the calculated change in thoracic blood volume is less than 10 to 15 per cent of the normal recumbent pulmonary blood volume.

B. *Circulatory Changes in Man and Intact Animals.*—The mean ballistic response of 10 human beings to 10 per cent O_2 and 6 per cent CO_2 is presented

*The authors are grateful to Mr. Henry Seeler, Aero-Medical Laboratory, for adapting his resuscitator to low flows suitable for animals.

in Fig. 2,*A*. Though hyperventilation increased force slightly and hyperventilation on 6 per cent CO_2 far exceeded that on 10 per cent O_2, force was uniformly higher with hypoxia and remained high despite definite hypoventilation during the first 5 minutes of recovery. Voluntary hyperventilation and CO_2-driven hyperventilation produced comparable increases in force, but the frequent observation of a further increase in the first minute of recovery from CO_2 suggested that factors other than hyperpnea were involved in the hypercapnic response. Alveolar O_2 and CO_2 tensions were estimated from the alveolar air equation assuming a dead space of 160 c.c., RQ of 1, and O_2 consumption of 310 c.c. per minute. From the calculated gas tensions a mean blood O_2 saturation of 66 per cent (range of 76 to 51 per cent) was indicated.[19] Force and saturation were inversely related in subjects less than 60 per cent saturated. Alveolar CO_2 tension did not exceed 48 mm. Hg, and in this range was not correlated with force.

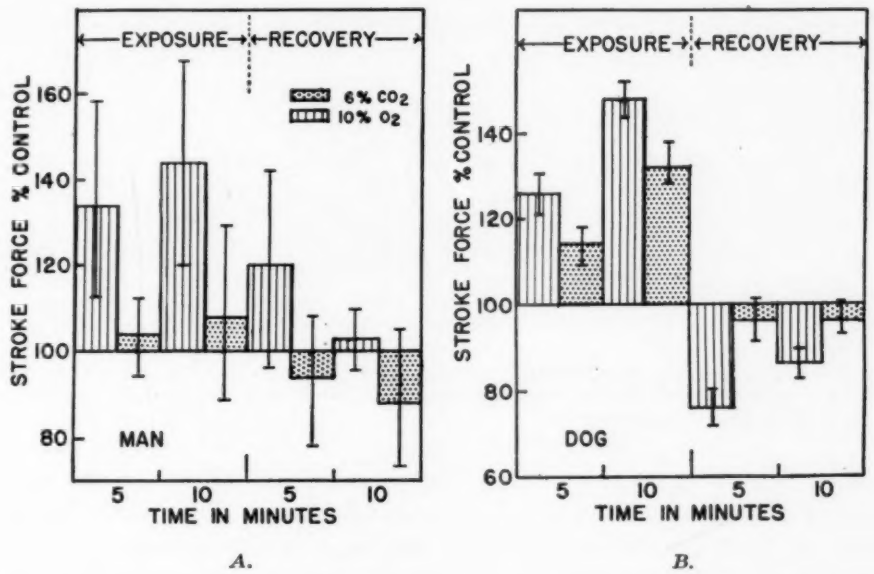

Fig. 2.—Mean ballistic responses of 10 normal, spontaneously breathing human beings and 5 anesthetized curarized dogs under constant ventilation. Vertical lines denote 1 standard deviation.

Fig. 2,*B* represents the mean of 10 observations on five dogs exposed to the same mixtures. The changes are larger and more consistent than in man because of constant ventilation, anesthesia, and the shape of the canine oxygen dissociation curve. The theoretical maximum O_2 saturation, probably unattained, was 50 per cent. Fig. 3 illustrates a typical hypoxic response. Peak force was attained within 7 minutes and subsequently decreased without falling below control. If epinephrine was administered as force declined, a secondary rise occurred, though the same dose elicited far greater change on 100 per cent O_2. Heart rate increased in five animals, decreased in three, and remained constant in one. Limb volume, pulse and diastolic pressures rose sharply, and both the anacrotic slope and the area beneath the pressure curve increased. There was no significant electrocardiographic change. Immediately after return to 100 per cent O_2, force,

pressure, and heart rate occasionally increased further, as in Fig. 3. This was followed by an impressive uniform decrease in force below control, maximal in 3 to 5 minutes, with complete recovery in 10 minutes. Limb volume decreased abruptly in the first 30 seconds on O_2 but stabilized above control volume; control heart rate and arterial pressure were regained within 2 minutes.

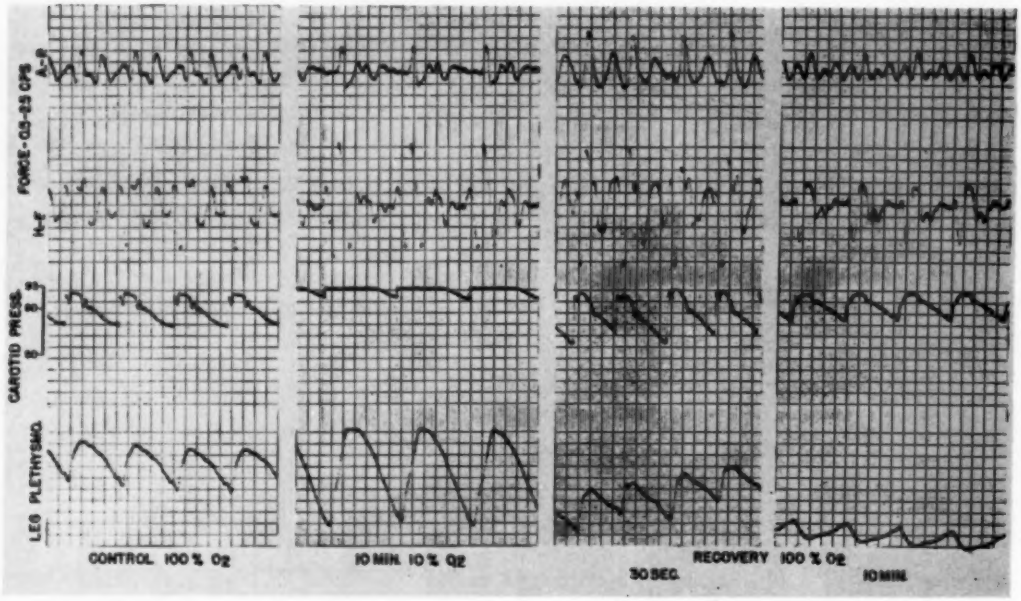

Fig. 3.—Force, pressure, and limb volume changes with hypoxia in a dog. Note the increase in force during exposure despite rise in diastolic pressure, the "overshoot" during early recovery, and the subsequent decline below control values.

Under 6 per cent CO_2, force, pulse pressure, and limb volume increased moderately without consistent change in heart rate or diastolic pressure. The effects of 10 to 30 per cent CO_2 were complex, and although the pattern of response was uniform, the degree of change varied considerably among the 6 animals studied (see Figs. 4 and 5). During the first two minutes, rate, force, diastolic and pulse pressures all declined. Within 3 minutes, however, force and pulse pressure began increasing, and diastolic pressure continued to fall. This secondary rise increased force above control in 4 animals on 15 and 20 per cent CO_2 and in one on 30 per cent CO_2. Heart rate decreased slightly and limb volume remained unchanged. Force increased abruptly in every animal on return to 100 per cent O_2 from 15 and 20 per cent CO_2, and in three animals on return from 30 per cent CO_2. A simultaneous overshoot in diastolic and pulse pressures occurred, but cardiac rate failed to exceed control. Unlike the hypoxic overshoot, force remained high for as long as 20 minutes.

C. *Mechanisms of Circulatory Changes.*—

1. *Role of centrally mediated reflexes:* Two animals were exposed to 10 per cent O_2 after spinal transection at the second cervical vertebra. Such preparations tolerate considerable stress, and although ballistic amplitude fell follow-

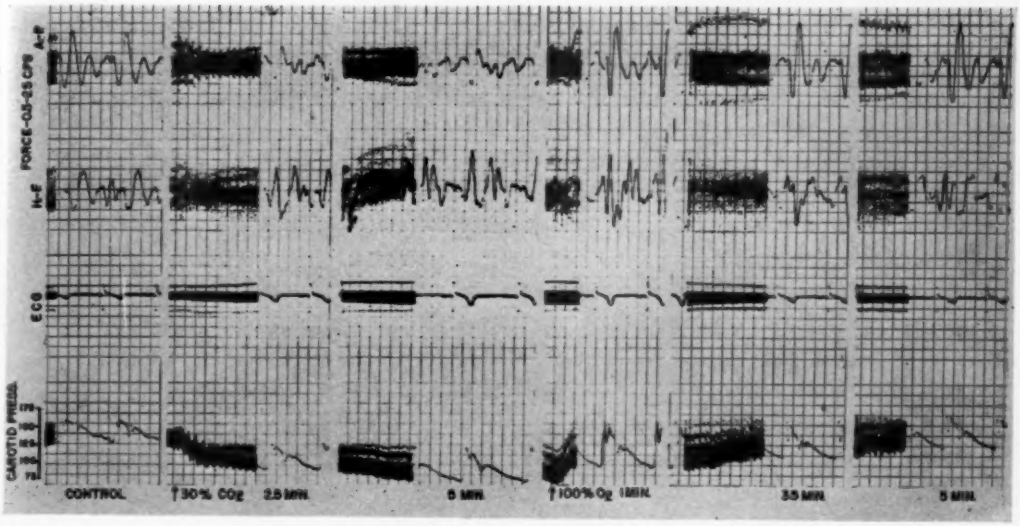

Fig. 4.—Effect of 30 per cent CO_2 on force and arterial pressure in an anesthetized dog under constant ventilation. The initial decline in force and pulse pressure is followed by a gradual rise despite continued exposure. The "overshoot" on return to 100 per cent O_2 is particularly striking in this animal.

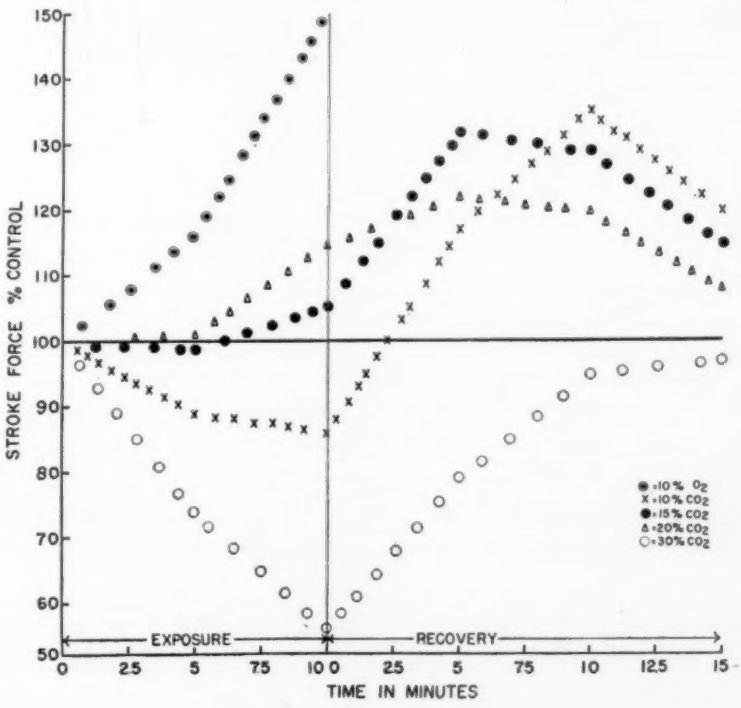

Fig. 5.—The effects of hypercapnia are contrasted with those of hypoxia in the same dog. After ten minutes of exposure the blood epinephrine titer was 0.033 mcg. per cubic centimeter breathing 10 per cent O_2 and 0.07 mcg. per cubic centimeter breathing 30 per cent CO_2.

ing surgery, wave form definition remained satisfactory. In contrast to the brisk increase observed in intact animals, force and limb volume decreased progressively to death at the seventh and eighth minutes of exposure. (See Fig. 6.)

Two animals known to increase force on 6 per cent CO_2 exhibited 5 per cent and 15 per cent decreases, respectively, following spinal transection. Pressure, limb volume, heart rate, and electrocardiogram remained unchanged. Force

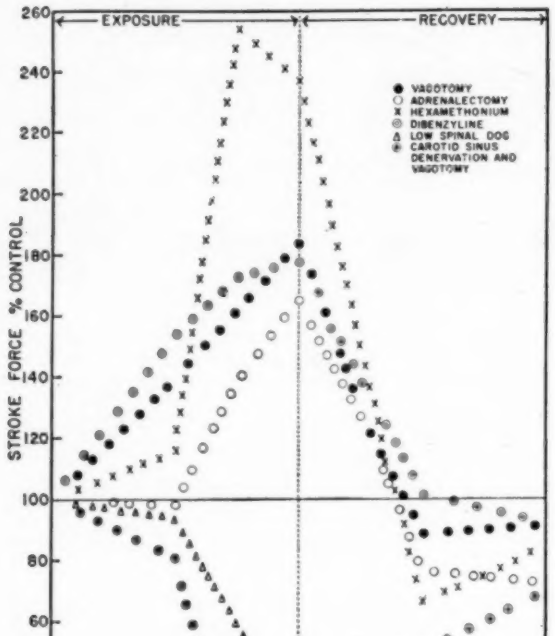

Fig. 6.—Effect of interference with autonomic function on the ballistic response to hypoxia. Discussion in text.

decreased to approximately half control in the first 3 minutes on 15 to 30 per cent CO_2 and failed to recover with continued exposure. Though the spinal animal is almost maximally vasodilated, both systolic and diastolic pressures decreased slightly and the Traube-Hering waves which were accentuated by CO_2 in the intact animal were abolished. On return to 100 per cent O_2 the normal abrupt increase in force and pressure failed to appear, and control values were not regained.

Successful adaptation is evidently centrally mediated, and in the absence of compensatory reflexes the separate direct depressant effects of hypoxia and hypercapnia are revealed.

2. *Importance of peripheral receptors:* Dautrebande[20] described a depressor reflex in spontaneously breathing hypercapnic dogs which was reversed by vagotomy or pulmonary denervation but not by section of the aortic depressor nerve. To ascertain the importance of such a reflex under controlled respiration, three

animals were exposed to 6 per cent CO_2 and one to 10 per cent CO_2, before and after bilateral cervical vagotomy. No change was observed in any parameter, and the hypoxic response was also unaffected.

To completely abolish chemoreceptor activity a 1 inch segment of vagus was resected bilaterally, the carotid arteries were stripped in the region of the sinuses and Hering's nerves severed. Such a preparation exposed to 10 per cent O_2 behaved precisely like a spinal animal. Capacity to adapt to hypercapnia, however, varied widely as indicated by the following extremes of responsiveness.

An animal known to increase force on 6 per cent CO_2 exhibited a 15 per cent decrease after chemoreceptor ablation. With higher concentrations force fell below half control and failed to recover with continued exposure. In contrast, another preparation tolerated up to 20 per cent CO_2 as though intact. On 30 per cent CO_2 pressure fell from 228/172 to 196/144 and force decreased 36 per cent in 3 minutes. Periodic concomitant increases in force and pressure then appeared resembling Traube-Hering oscillations but far greater in amplitude and duration. Oscillation frequency and mean force and pressure rose gradually until normal adaptation was duplicated once more.

3. *Role of the sympathoadrenal system:* Epinephrine release is of proved importance in anoxia and asphyxia, and CO_2 is known to excite sympathetic centers.[1-7] It therefore seemed probable that the sympathoadrenal system mediated adaptive responses to both hypoxia and hypercapnia.

Sympatholytic drugs are thought to block carotid and aortic receptors, and sympathetic ganglionic transmission.[21,22] In an attempt to eliminate the sympathoadrenal system pharmacologically, 4 animals were exposed individually to 10 per cent O_2 and 6 per cent CO_2 before and after 6 to 16 mg. of hexamethonium per kilogram body weight. Paradoxically, a dramtic increase in cardiac responsiveness to hypoxia was elicited as indicated in Fig. 6, and contraction of the nictitating membrane was not prevented. The response to 6 per cent CO_2 was unchanged. In two additional dogs dibenamine and dibenzylene failed to modify the ballistic responses to either hypoxia or hypercapnia despite vasodilation and inhibition of contraction of the nictitating membrane. Histaminic adrenal stimulation was investigated by exposing an animal to 10 per cent O_2 after 5 mg. of Benadryl per kilogram body weight. As expected from the behavior of the denervated preparations the hypoxic response was unchanged.

Bilateral adrenalectomy also failed to change the circulatory reponse to 6 per cent CO_2 or 10 per cent O_2 in dogs, and vigorous contraction of the nictitating membrane after bilateral adrenalectomy was observed in two hypoxic cats, emphasizing the importance of extra-adrenal chromaffin tissue.

Premedication with epinephrine minimized or prevented the depressant effects of 10 per cent O_2 and 30 per cent CO_2 on spinal animals, and the ballistic effects of hypoxia and hypercapnia prior to spinal section were largely reproduced by 30 to 50 mcg. of epinephrine. In three assay cats hypertension and contraction of the nictitating membrane began in 2 to 3 minutes, and in 10 minutes an output of from 1.5 to 7.0 mcg. was observed. Because of its direct relaxant effect on smooth muscle, CO_2 decreases the responsiveness of the nictitating membrane relative to its calibration on 100 per cent O_2, thus minimizing estimated epine-

phrine production. Nevertheless, contraction was occasionally observed on 6 and 10 per cent CO_2, appeared regularly on 15 per cent, increased on 20 per cent, and at peak response to 30 per cent CO_2 corresponded to 4 to 6 mcg. To obviate species differences, heparinized venous samples were obtained in three dogs at peak ballistic response to 10 per cent O_2 and 30 per cent CO_2, immediately chilled and centrifuged, and 3 c.c. of plasma were injected rapidly intravenously into assay cats. The membrane did not react to plasma obtained from fully oxygenated dogs. Membrane contraction was observed in but one such experiment, and corresponded to 0.033 mcg. per cubic centimeter on 10 per cent O_2 and 0.07 mcg. per cubic centimeter on 30 per cent CO_2, values barely within the range of sensitivity of the method. Fig. 5 displays the corresponding ballistic responses. Note that force increased 52 per cent during hypoxia, but was decreased 45 per cent by CO_2 despite the higher epinephrine titer.

4. *Importance of pH:* To determine the specificity of circulatory response, 500 c.c. of N/10 acid were rapidly infused into two dogs. Though slight increases in force and limb volume were observed, the effects were in no way comparable to those of hypoxia or hypercapnia, a conclusion previously expressed by Gremels and Starling.[9]

DISCUSSION

Significance of the Method.—The above experiments illustrate the potential danger in interpreting pressure change as vasomotion without knowledge of cardiac function. The ballistocardiogram provides such information, for the amplitude of one of its deflections is proportional to the cardiac determinants of pressure. Similarly, ballistic amplitude may not be interpreted in terms of contractility without knowledge of vascular tone.[16] Together, the ballistocardiogram and arterial pressure measurements provide interrelated data on the relative contribution of pump and conduits to the maintenance of the circulation.

Blood Volume Distribution.—In pharmacologic experiments it is important to know whether change in contractility is a direct effect or the result of passive change in ventricular filling.[23] Measurements of thoracic blood volume are useful in this regard for the pulmonary reservoir modulates secondary changes in diastolic volume.[24,25] In animals, the effect of hypoxia and hypercapnia on the pulmonary reservoir is controversial[26-28]; in man hypoxia is without effect, and the action of CO_2 unknown.[29,30] It is therefore of interest that no significant change in thoracic blood volume was observed in man with either 12 per cent O_2 or 6 per cent CO_2 using the teeterboard technique.

Circulatory Effect of Hypoxia.—Cardiac output increases beyond a threshold arterial unsaturation of 45 per cent in anesthetized dogs[31,32] and 18 per cent in unanesthetized normal man[33]; stroke acceleration also increases in hypoxia.[31] Since both determinants of force were augmented by hypoxia, the uniform increase which we observed was expected, and has been previously reported.[34-36] The mechanism by which the body accomplishes so salutary a hyperkinesis, however, has not received sufficient attention.

Intact spontaneously breathing dogs tolerate 10 per cent O_2 for several hours,[32] despite the extreme sensitivity of cardiac muscle to oxygen lack.[9,10] Hypoxic spinal and chemoreceptor denervated preparations, however, rapidly

developed circulatory failure,[37,38] due in part to loss of contractility, as indicated by decreased reaction force. Stavraky[38] has observed hypotension and syncope in human beings resuscitated from severe hypoxia with 100 per cent O_2, and attributed the reaction to medullary depression unmasked by elimination of chemoreceptor drive with oxygen. The marked decrease in force as our intact animals were reoxygenated probably represents a similar phenomenon and illustrates chemoreceptor control of contractility.

Cannon[1] and others[6,7] have described the stimulant effects of hypoxia and asphyxia on adrenal secretion, and the complementary role of sympathicotonia has been emphasized by Gellhorn[2] and Celander.[5] In the present study, hypoxia uniformly augmented ballistic amplitude, peripheral blood flow, pulse and diastolic pressure, responses which could be duplicated in the spinal animal by a suitable dose of epinephrine. Hypertension and contraction of the nictitating membrane were elicited in cats ventilated on 10 per cent O_2, and an elevated epinephrine titer was demonstrated in intact dogs by bioassay of venous blood. There seems little doubt that chemoreceptor activity effects a sympathoadrenal discharge responsible for successful adaptation. The contrary conclusion of Van Loo, Surtshin, and Katz[8] was probably based on inadequate methods.

Decreased force and loss of epinephrine sensitivity with prolonged exposure is clarified by the work of Ellis[39] which indicates that epinephrine facilitates conversion of energy to mechanical work, without altering energy production. In this view, epinephrine improves contractility to the extent that decreased energy production can be compensated by increased efficiency of energy utilization.

Experiments purporting to eliminate the effects of epinephrine pharmacologically or surgically frequently appear in the literature.[8,40] It is therefore important that neither chemoreceptor discharge nor release of epinephrine were prevented by hexamethonium, nor were the cardiac effects of sympathetic amines inhibited by dibenamine or dibenzylene. Pate and Taylor[41] reported augmented pressor responses to epinephrine following ganglionic blockade, and attributed the phenomenon to loss of vasomotor control. Enhanced ballistic responses to hypoxia after hexamethonium suggest that the phenomenon may also be related to increased cardiac contractility. Reflex epinephrine release following adrenalectomy has been observed repeatedly,[6,37,38,42] and in our experience failed to diminish epinephrine release in cats or the circulatory response of dogs to hypoxia. These observations and those of Malméjac[43] suggest the existence of a servomechanism responsible for regulating total body chromaffin activity in accordance with epinephrine output.

Circulatory Effect of Hypercapnia.—Interest in hypercapnia has been stimulated by the realization that alveolar CO_2 tensions equivalent to inspired concentrations up to 30 per cent CO_2 in O_2 are encountered in anesthesia,[44] by the use of hypercapnia in psychotherapy,[45] and by its growing importance to military medicine.

Discrepancies between the published results of careful investigators[20,37,40,44,46,47] emphasize the importance of species, anesthesia, CO_2 concentration, type of respiration, duration of exposure, rate of change of CO_2 tension, and presence of anoxia. Our conclusions pertain to brief exposures of

anesthetized, curarized, fully oxygenated dogs and cats from 6 to 30 per cent CO_2 at constant ventilation, and to unanesthetized man breathing 6 per cent CO_2 in O_2.

Ketcham, King, and Hooker[46] found that the isolated mammalian heart fails when its perfusate is equilibrated with as little as 3 per cent CO_2. The contrary results of Jerusalem and Starling[48] using the heart-lung preparation were based on failure to eliminate secondary factors.[47] In our own experiments, force decreased uniformly in hypercapnic spinal animals and failed to recover with continued exposure or to overshoot with reoxygenation.

Despite its direct depressant action 6 per cent CO_2 increased force independently of rate, ventilation, or thoracic blood volume in man, and a comparable response in intact dogs persisted after ganglionic and adrenergic "blockade," vagotomy, and adrenalectomy. Under 10 to 30 per cent CO_2 ballistic amplitude appeared to vary with the balance between stimulant and depressant influences. Force, rate, and diastolic pressure initally decreased, but after 10 minutes' exposure regained or exceeded control values, and increased still further with reoxygenation. From the purely mechanical standpoint, force and resistance are inversely related.[16] During hypercapnia, however, they varied directly, indicating that contractility also changed. Quantitative variation in ballistic response, therefore, reflects individual differences in vasomotion relative to contractility change, as well as the extent to which homeostatic resources are employed.

The afferent pathway responsbile for mobilizing adaptive resources is controversial. Dautrebande[20] reported that chemoreceptor ablation augmented the toxicity of 20 to 40 per cent CO_2. Cardiac function was not measured and the experiments were interpreted as a direct vasodilator effect of CO_2. Gellhorn[2] and Page and Olmsted[40] were unable to reproduce these results. We found the initial depressor response to hypercapnia enhanced by the absence of chemoreceptors. The degree of compensation during continued exposure, however, varied between normal behavior and that typical of spinal preparations. It is of interest that in one animal adaptation to 30 per cent CO_2 took the form of surging increases in force and pressures. Starling[49] attributed augmented Traube-Hering oscillations to depression of the vasomotor center and compared them to the tremor of a fatigued muscle. Rhythmic change in force and pressure, therefore, suggests attempted compensation by a depressed vasomotor center handicapped by lack of chemoreceptor drive. The fact that ballistic amplitude exhibited parallel fluctuations demonstrates that the vasomotor center augments contractility as well as vasomotor tone.

The effector of hypercapnic adaptation is also the subject of controversy. Kellaway[6] reported failure to demonstrate epinephrine release with up to 16 per cent CO_2, though his protocols suggest an opposite conclusion. Houssay and Molinelli[7] were also unsuccessful, but direct CO_2 effects on their test objects might have obscured a positive response. Gellhorn[2] cites the above authors in strongly denying hypercapnic epinephrine release. On the other hand, Mackay[50] observed hyperkalemia and Schaefer[51] hyperglycemia with narcotic concentrations of CO_2, and commented on the possible role of epinephrine in producing these changes.

Our experiments furnish decisive evidence of a vital function of epinephrine in adaptation to hypercapnia. Epinephrine ameliorated established CO_2 toxcity, and premedication abolished the supersensitivity to CO_2 of spinal and some chemoreceptor denervated preparations. In cats, contraction of the nictitating membrane occurred regularly with 15 to 30 per cent CO_2, and a high titer of epinephrine was demonstrable in a dog at peak response to 30 per cent CO_2. In view of the decrease in epinephrine output with barbiturate anesthesia,[17] it seems likely that the response of unanesthetized human beings to 6 per cent CO_2 may also be due to epinephrine discharge.

SUMMARY

1. Mechanisms responsible for circulatory changes in hypoxia and hypercapnia have been studied with an "aperiodic" ballistocardiograph, teeterboard, and ancillary techniques. The results emphasize the necessity for measuring cardiac function in evaluating the effects of drugs or autonomic discharges, for both the vasomotor center and chemoreceptors altered ventricular contractility as well as vasomotor tone.

2. In man, no significant change in thoracic blood volume was demonstrable in response to 10 per cent O_2 or 6 per cent CO_2.

3. Contractility increased on 10 per cent O_2 but decreased steadily when reflex compensation was prevented by spinal transection. Peripheral chemoreceptors constituted the afferent limb and epinephrine the chief effector of this reflex. Cardiac depression occurred on return to 100 per cent O_2 and may be important in the circulatory collapse which sometimes follows abrupt reoxygenation in man. Neither adrenalectomy nor adrenergic "blockade" prevented the positive inotropic response to hypoxia, and hexamethonium paradoxically sensitized the heart to epinephrine. The significance of these observations is discussed.

4. In cats, an epinephrine discharge occurred regularly with inspired CO_2 concentrations in excess of 15 per cent in O_2, and in dogs epinephrine was demonstrable in venous blood at peak ballistic response to 30 per cent CO_2. Though mild hypercapnia (6 per cent) increased ballistic amplitude in both dog and man, severe hypercapnia (15 to 30 per cent) markedly depressed the heart until reflex epinephrine discharge restored contractility toward normal. Chemoreceptors were not uniformly necessary, but adaptation seemed facilitated by their presence.

5. Circulatory performance in hypoxia and hypercapnia represents the resultant of direct cardiac depressant effects and opposing reflexly mediated alterations in contractility and vascular tone.

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THE TOTAL QRS DURATION

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THE QRS duration in the electrocardiogram is measured routinely in Limb Leads I, II, III, aV_R, V_L, V_F, and the longest value in any of these leads is accepted as the most nearly correct.[1] Wilson and Herrmann[2] pointed out in 1930, that QRS duration in a single lead was incorrect, in that vectors of early or late ventricular activation might be perpendicular to the lead derivation and, thus, isoelectrically recorded. It is now equally evident that vectors of early and/or late activation may occur in a plane more or less perpendicular to the entire frontal plane and not be registered maximally in limb leads at all (Fig. 1). Many investigators[3,4,23,25,34] have shown that longer QRS duration values obtain in horizontal plane (precordial) leads. Rapaport, Bierman, Sokolow, and Edgar[3] measured longest QRS duration in Leads V_1 and V_2 in simultaneous fast-speed recordings of standard limb and precordial leads. Kissin and Schwarzschild[4] have apparently been alone in suggesting that the longest QRS duration in any electrocardiographic lead be employed as the more nearly correct.

In probably the most thoughtful article extant on QRS mensuration, Lepeschkin and Surawicz[5] discuss the difficulties of accurate QRS duration measurement in clinical electrocardiograms. They list the sources of error as the absence of spatial correction, phase differences in single lead records, beat-to-beat variability, and the determination of the end point along the terminal part of the QRS curve. These technical impedimenta, plus the large accumulation of empirical limb lead data, have probably discouraged the systematic study toward more accurate QRS measurement, and the attainment of "normal standards" closer to true QRS duration.

It seems reasonable at this time to apply principles of spatial vectorcardiography to the study of electrocardiographic time intervals, employing a triaxial XYZ lead system, sensitive fast-speed, multichannel recording, and other techniques to reduce measurement error. The clinical problems dependent upon QRS interval measurement in the electrocardiogram require no elaboration. It is possible that accurate recording and interval measurement may elicit new and fundamental information, particularly concerning beat-to-beat QRS variability, which is impossible of delineation by conventional techniques.

This study is an attempt to measure total QRS duration as accurately as is now possible and to establish tentative standards for the spatially corrected param-

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eter in healthy male adults. Some of the factors involved in physiologic and pathologic variability of QRS duration will be discussed.

METHOD

From studies of high fidelity electrocardiograms by Langner[6] and by Kerwin,[7] it appears that a certain minimum frequency response, amplification, and paper speed, far exceeding specifications of most scalar recorders in this country, may be necessary for faithful reproduction of the electrocardiogram. In this study the Swedish twin-channel, jet-writing Mingograf was

Fig. 1.—Horizontal plane loop demonstrating early and late QRS vectors perpendicular to frontal body plane.

employed. Its frequency response is claimed to be linear to 500 cycles per second, with frequencies to 900 cycles registrable. The observed deflection time is approximately 2 msec. as seen in the standardization pulse applied at 100 mm. per second paper speed (Fig. 2). The paper speed was readily and frequently verified by introduction of 60 cycle interference. The time constant of the amplifiers is approximately 2 seconds. A. C. interference was reduced by vigorous preparation of the skin with a moist, warm, rough cloth, by recording during quiet breathholding, by shortening of lead loops, and by optimal grounding. Electrodes were ovoid shaped, of 4 by 5 cm. dimensions. Standard amplification (1 cm. = 1 mv) was used, as other conventional type ECG measurements were anticipated for these records. No significant difference in QRS duration was found in records taken at amplifications of 1 mv = 1.0 cm., and 1 mv = 1.5 cm. (means 82.1 vs. 83.8, t 1.0 vs. 1.5 = 1.384, $P_t = 0.18$).

Recordings were made on 115 clinically healthy men, ages 20 to 50 years, who were on active duty with the U. S. Naval Air Forces. The subjects rested supine for 15 minutes while electrodes were applied, the procedure explained, and recording stabilized. An anatomically orthogonal XYZ lead system was employed. Bipolar electrodes were placed as follows: a horizontal component, X_r was derived from electrodes at each midaxillary line in a plane at the level of the fifth intercostal space in the midclavicular line. The vertical Y lead was derived from an electrode in the same horizontal plane at a left parasternal position and from a forehead electrode. The sagittal lead was taken from the same horizontal plane at a right parasternal position to an anatomically opposite point in the right interscapular area. A simultaneously recorded time-reference peak was derived from any anterior chest position which produced a good, sharp timing peak. A comparable system of electrode placement for XYZ bipolar leads has been shown in model studies to give a good approximation to electrical orthogonality,[8] and the present arrangement is satisfactory for ECG interval studies. Records of 4 to 6 beats were made during quiet breath-holding at the end of normal expiration.

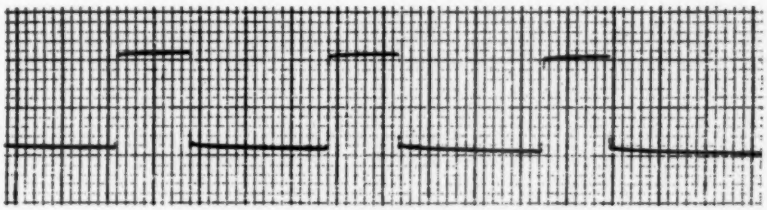

Fig. 2.—Mingograf deflection time.

Paper strips of 4 to 6 beats in each lead were mounted on manila sheets and enlarged 10 times by projection upon a fixed screen. The constancy of enlargement was controlled by superposing a centimeter ruler on the projected image of the millimeter paper co-ordinates. One centimeter on the image represented 1 mm. or 10 msec. on the original record. For the tracing of each QRS curve a ruled paper was attached to the screen, its lines arranged parallel to those of the projected co-ordinates. The desired QRS complex and its time-reference peak were centered, and a fine, hard-pencil tracing drawn vertically through the time-reference peak (Fig. 3). A fine pencil tracing of the beginning and the end of the QRS complex was made along the midaxis within the curve tracing. The record base line averaged 4 mm. wide in the projected image. Straight line extensions were made of the straight segment along the P-R and ST base lines (Fig. 3).

Determination of earliest and latest deflections in any recording system must be made taking into consideration the base-line width and the "noise" of the recording, as well as the sensitivity of the instrument. The deflection time of the Mingograf is such that base-line width is the more important factor in establishing significant points along the curve of early and late activation. It was considered reasonable to elect a deflection from the midaxis of the base line representing a distance of half the tracing width as the first or last consistently measurable point. This departure distance from the base line allowed excellent reproducibility of measurement, and was feasible, due to the fine, jet-line tracing and to interference being largely confined to the width of the ink line. In virtually all cases, a straight segment was found along the ST-T curve in these records from which to plot the end of QRS activity. The straight segment was not necessarily horizontal, however, due to displacement by rising potentials of recovery. The P-R segment is, of course, almost uniformly flat.

The distance of half-tracing width from the base line (usually 2 mm. in the enlarged image) was established along the beginning and terminal curves. A perpendicular was dropped from these points to the time-reference line and the QRS duration read off directly in milliseconds (Fig. 3).

The total QRS duration from XYZ leads was determined by the longest interval from onset of activity to the time-reference peak in any XYZ lead, added to the longest interval from this reference line to end of activity found in any XYZ lead. The mean total QRS duration was derived from the average of 2 total QRS durations measured in simultaneous XYZ leads. The QRS duration for simultaneous standard Leads, I, II, and III was measured in the same manner in 24 subjects. Error of measurement was on the order of 2 msec., measured as the standard deviation of the individual differences from the mean of repeat QRS measurement in the same record. Error of measurement by identical criteria was on the order of 0.5 msec. in QRS duration measured in single leads.

In a small group of subjects both resting and postexercise tracings were performed.

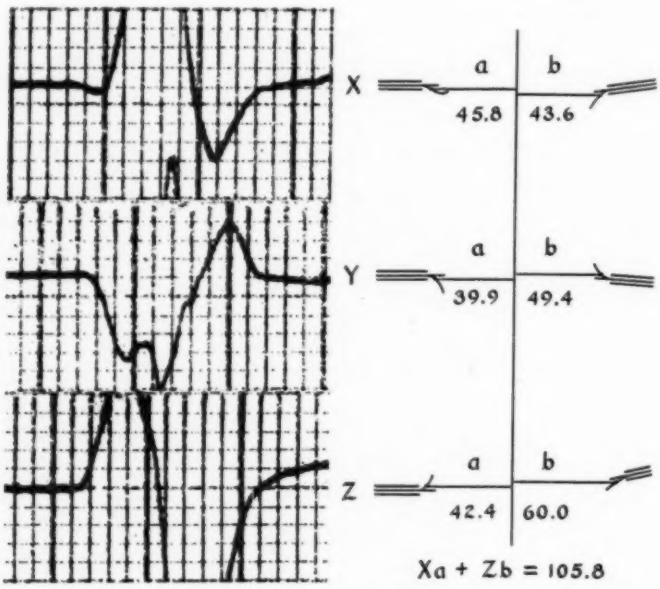

Fig. 3.—Diagrammatic presentation of total QRS duration measurement technique from earliest to latest QRS deflections.

RESULTS

In this group of 115 men, ages 20 to 50 years, the mean of the individual QRS duration values was 101.0 msec. (0.1010 second) with a standard deviation of 10.4 msec. (Table I).

TABLE I. TOTAL QRS DURATION IN 115 MALES

Range:	0.0801 to 0.1309 second
Mean:	0.1010 second
S.D.:	0.0104 second
> 0.10 second	54.0%
> 0.11 second	18.0%
> 0.12 second	3.5%
> 0.13 second	0.9%

The frequency distribution of total QRS duration values is presented in Fig. 4, and is obviously moved towards higher values than those found in limb leads. The shortest QRS duration observed was 80.1 msec., the longest 130.9 msec. No pattern of block was present in any of the 115 subjects. Fifty-four per cent of

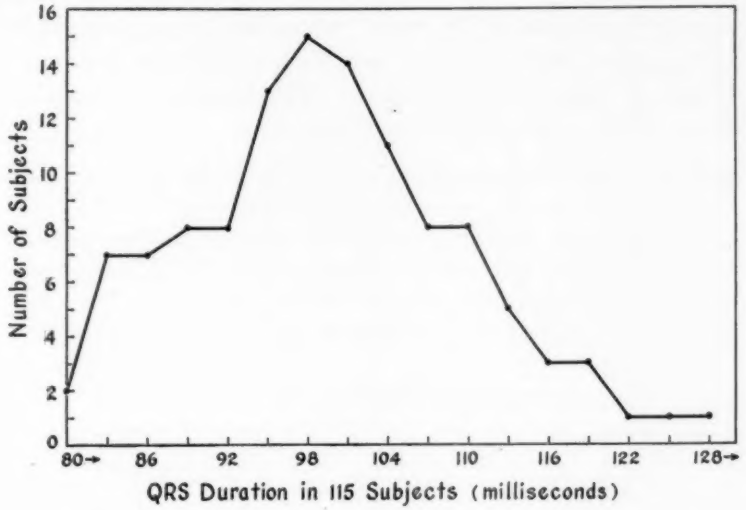

Fig. 4.—Frequency distribution curve of total QRS duration from XYZ leads.

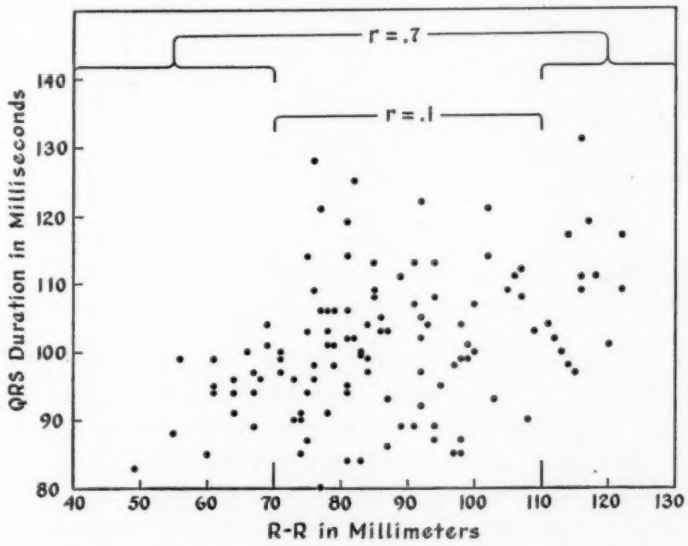

Fig. 5.—Relation of total QRS duration and heart rate.

values fell above 0.10 second, the conventional "upper normal limit" in standard limb leads. Eighteen per cent were above 0.11 second, and 3.5 per cent above 0.12 second.

In a compilation of mean QRS duration values from the largest and some of the more reliable "normal" series, a weighted mean QRS duration of 85.8 msec.

was found.[16,31-35] There is a highly significant difference between the mean of conventional values in limb leads and those in XYZ leads ($t = 10.07$) ($P = < 0.001$).

Table II shows the QRS duration observed in simultaneous standard limb Leads I, II, and III of 24 subjects, measured by the same technique from earliest to latest deflections in any lead. These values are compared to the total QRS duration values derived from XYZ leads. In no instance was the QRS duration longer in frontal plane records. The correlation coefficient was 0.71 between these two groups of values. The range of QRS duration in simultaneous limb leads was 76.5 to 109.0 msec., the mean 90.4 msec.

TABLE II. QRS DURATION IN LIMB VS. XYZ LEADS IN MILLISECONDS

I, II, III	X, Y, Z
100.7	118.9
94.5	108.5
90.6	99.3
89.5	110.9
79.6	86.8
109.0	130.9
84.8	93.7
84.1	104.0
97.0	103.3
86.0	95.0
95.6	101.0
76.5	84.6
106.5	108.7
91.3	98.7
78.5	107.5
78.6	102.3
90.6	104.9
84.2	85.5
89.0	90.7
85.2	106.3
88.1	100.2
108.1	124.5
87.0	101.3
93.5	99.9

Correlation coefficient I, II, III vs. X, Y, Z — r : 0.71.

In Fig. 5 the relationship between heart rate and total QRS duration is plotted for all subjects. The correlation is highly significant at the extremes of heart rate. Rate was eliminated as a physiologic variable in calculating other correlations for the group in the rate range corresponding to an R-R interval of 0.70 to 1.1 seconds, representing 75 per cent of the subjects.

No significant correlation was found between body weight and QRS duration ($r = 0.08$). Mean weight of the group was 174 pounds, standard deviation 26 pounds.

No correlation was observed between age and QRS duration ($r = 0.00$). Mean age was 32 years, standard deviation 6 years.

In 30 per cent of the subjects the total QRS duration occurred in the sagittal Z lead alone. The correlation between QRS duration in the Z lead and total QRS duration for all subjects was 0.7, some correlation having been expected for a part representing a large proportion of the whole value. Earliest and latest

activity in the X lead alone occurred in only 9 per cent of the subjects, and in the Y lead in 10 per cent. The occurrence of both early and late vectors in a single lead suggested a possible relationship to the configuration of the QRS loop or the direction of its mean vector. A crude vector analysis of the XYZ patterns indicated that in the group with both early and late vectors recorded in the sagittal Z lead, there was more likely to be a posteriorly directed mean QRS vector (54 per cent compared to 37 per cent of the entire group). Cases in which both early and late vectors occurred in the X lead alone showed most frequently an anteriorly directed QRS vector (80 per cent compared to 27 per cent of the entire group). In records showing maximum duration in the vertical Y lead alone no consistent vector orientation was ascertained.

QRS Duration and Exercise.—Ten subjects were exercised by a maximally rapid series of steps on a 16 inch step, over a period of one and one-half minutes, with electrodes in place. Postexercise records were made immediately and at 5 minutes. In Table III the change in rate and in QRS duration is tabulated,

TABLE III. QRS DURATION AND EXERCISE

RESTING QRS (MILLISECONDS)	EXERCISE QRS (MILLISECONDS)	DIFFERENCE	RESTING R-R	EXERCISE R-R
94.3	97.3	+3.0	67	70
88.8	92.3	+3.5	94	94
99.4	103.2	+3.8	84	81
112.6	113.3	+0.7	91	80
117.4	122.5	+5.1	114	98
85.0	91.4	+6.4	74	70
112.1	113.6	+1.5	107	88
96.7	105.5	+8.8	115	112
110.9	115.4	+4.5	116	102
100.7	108.7	+8.0	78	75

TABLE IV. VARIABILITY OF QRS DURATION IN CONSECUTIVE BEATS (MILLISECONDS)

BREATHHOLDING	BREATHING
81.6	78.2
80.2	80.8
80.9	78.7
78.8	79.8
78.9	84.9
81.1	82.1
79.7	80.1
83.8	78.5
84.6	82.7
81.1	81.4
$\bar{x}$ = 81.1	$\bar{x}$ = 80.7

$F = 1.241$
$F_{.05} = 2.22$

Difference in beat-to-beat variability nonsignificant.

showing a significant ($p = < 0.001$) and uniform lengthening of QRS duration immediately after exercise in the presence of an increased rate.

Beat-to-Beat Change.—Beat-to-beat QRS variability in individual leads was determined during quiet breathing as compared to breathholding (Table IV). There was no greater variability between beats during breathing than during breathholding. Mean variability in single leads was on the order of 2 msec., while mean variability in total QRS duration from simultaneous XYZ leads was 3 msec.

Attempts made to vary heart size by Valsalva and Mueller experiments resulted in unsatisfactory tracings with skeletal muscle potential interference.

DISCUSSION AND CONCLUSIONS

As expected, the upper and mean values of QRS duration measured in XYZ leads by this method were found to be greater than those from conventional limb lead measurements. The lower limit of values (0.080 second) was moved upward, as well. It was unexpected that a very small incidence of high values (over 0.12 second) was obtained. The criteria for selecting the points of beginning and ending of the QRS along the deflection are as realistic as feasible with available apparatus.

It is proposed that 0.12 second be the "upper normal limit" for QRS duration in simultaneous XYZ leads. The occurrence of 30 per cent of longest QRS duration values in the sagittal Z lead would suggest V_1 or V_2 as the single conventional lead in which the longest QRS duration might be most often measured.

The uniformly shorter QRS duration found in single or simultaneously recorded limb leads indicates that total QRS duration is measurable in these leads only by uncommon chance, if at all. The correlation of limb lead with XYZ lead values ($r = 0.7$) does not permit individual prediction of total QRS duration from limb lead measurements.

The longest QRS duration measurable in any of the 12 conventional leads is suggested as the more nearly correct value for single-channel scalar records, but the difficulties of accurate measurement in such tracings are emphasized by the method used in this study. The simultaneous recording of selected leads such as V_1, V_6, and aV_F might give the most nearly correct value obtainable from conventional leads, but this was not investigated. It is suggtsted that the earliest and latest consistently discernible deflections be selected for QRS interval measurement in future XYZ systems, rather than points in the mid-arc, or others chosen to give values closely comparable to present conventional standards.

QRS Duration and Heart Rate.—The QRS duration is generally considered the most stable item of the ECG with regard to changes in heart rate. A relationship between these two items would be of obvious clinical significance in determining upper limits of "normality," diagnosing intraventricular block, or determining abnormal response of QRS duration to exercise.

Reports on this relationship are at variance, though the results of previous measurements of QRS duration are not likely to be applicable to this study.[9-14] A significant relationship ($r = 0.7$) was found at the extremes of heart rate, but

through the usual range (R-R 0.7 to 1.1) rate and QRS duration were independently variable.

QRS Duration and Age.—Savilahti[12] and others showed a gradual prolongation of QRS duration from birth to adolescence, and as Lüderlitz,[15] and Glasser,[11] found no age trend in adults. Values in advanced age are not available. In the age range from 20 to 50 years of the present study, no age trend was found, although the spread in ages was not sufficiently great.

QRS Duration and Body Size.—X-ray estimation of heart size was not possible in this study. There exists, however, a direct relationship of heart size to body weight.[17] No significant correlation ($r = 0.08$) was found in this study between duration of QRS and body weight. Since QRS duration depends on the length of the conduction system and the myocardial mass activated, a closer correlation might have been expected. There is a considerable body of data supporting a relationship of QRS duration to heart weight in abnormal hearts, but no convincing correlation within the range of normal heart weight.[2,16,21,22,23,25] Mean QRS duration in limb leads was found to be longer in men than in women,[18,33] and mean heart weight in men was 312 grams, in women, 225 grams.[19]

Wilson and Herrmann[2] found an increase in QRS duration uniform with the heart weight and ventricular wall thickness found in autopsy. Schaefer[20] estimated a 5 msec. prolongation of QRS duration with a 5 mm. lengthening of cardiac fibers. He agreed with Wilson and Herrmann that an increase in muscle conduction time was insufficient to account for all QRS duration increment in heart disease, and that a change in the specialized conduction system time was always associated. Pardee,[21] Fahr,[22] and Myers[23] found a general relationship between QRS duration and the degree of cardiac hypertrophy. It was amusingly demonstrated by King, Jenks, and White[24] that a gross relationship existed with the gross increase in body size of animals, from mice to whales and elephants. The discrepancy between an approximately twofold increase in QRS duration from birth to adulthood in human beings and an eightfold increase in heart weight and a tenfold increase in heart length is not explained. Nor are the wide individual differences in QRS duration apparently unrelated to length or mass of the ventricles. It is supposed that the increased cross-sectional area of conduction fibers increases the conduction velocity in adult over infant hearts.[25]

QRS Duration and Exercise.—Schellong and Lüderlitz[26] employed QRS duration changes with exercise as a crucial part of a cardiovascular fitness test. Utilizing high-speed recording of a single bipolar chest lead, they demonstrated shortening in QRS duration of at least 2 msec. after exercise in 91.5 per cent of 83 subjects free of cardiovascular disease. They observed no change of QRS duration in 2.5 per cent. In an undetermined number of cardiac patients they uniformly found either no change or a prolongation of QRS duration after exercise. In an illustration of a tracing (abb. 26) in their monograph, there was a directional change in the QRS vector in the single lead recording which might, in itself, invalidate their conclusion of a change in total QRS duration. Their work was criticized by Neftel[27] and Reindell[28] both on the basis of the small error of measurement (2 msec.) which could not be repeated, and on the finding

of a shortening of QRS duration of 2 msec. or more in 40 to 50 per cent of proved cardiac patients. Neftel and Reindell found a significant prolongation of QRS duration in only 10 per cent of cardiac patients. There was insignificant QRS change in 50 per cent of normal subjects. This indicated a nonspecificity of the QRS change in exercise which, to the critics, invalidated the entire test for cardiovascular fitness.

Lepeschkin,[25] and Scherf and Schaffer[29] state that a small decrease in QRS duration occurs with exercise, a decrease which is usually related to rate change and which can only be measured with high-speed records. The shortening of QRS is attributed to more rapid intraventricular conduction from increased sympathetic tone, and to a possible decrease in ventricular volume.

The values in Table III are not in agreement with prior reports on QRS duration change with exercise. In spite of an almost uniform acceleration of rate, a mean lengthening of QRS duration for the group was observed, and found to be significant at the < 0.001 level. The exercise test was performed immediately after the resting record, and all measurements made at one sitting. Conditions of exercise are, of course, rarely comparable in any two studies, because of the different type of exercise employed.

Gross increase in QRS duration has been observed to occur with the development of bundle branch block at critical heart rates.[30] It would be most difficult in clinical tracings to detect small increments in QRS duration if they existed preceding the block pattern. It is conceivable that combined rate and myocardial changes prolong conduction time, and that these changes may occur normally. This may not invalidate the use of careful QRS mensuration as a basis for an exercise-tolerance test, since one might expect further QRS prolongation in myocardial disease.

Beat-to-Beat Variability in QRS Duration.—QRS duration variability between beats has been previously measured as 3 to 6 msec. in single leads with fast-speed recording.[25] It is speculative how much of this variability is "positional," and how much is related to autonomic nervous activity, phasic impedance variance from lung and thorax volume changes, myocardial impedance, or filling size changes.

It is most interesting that the beat-to-beat variability in long single lead strips taken during quiet breathing was no greater than that in beats taken during relaxed breathholding. Vectorial changes during quiet breathing are, of course, not great.

The mean variability between total QRS duration measurements was 3.3 msec. which probably represents beat-to-beat change in the three-dimensional system. This variability was measured with finer accuracy in single lead strips, where it was on the order of 2 msec. It must be appreciated that values for total QRS duration in this study were unavoidably derived from 3 individual beats, leads made isochronous with simultaneous time-reference peaks.

It is evident that the technique described is quite accurate for measuring beat-to-beat QRS duration changes in single leads, and mean changes in total QRS duration from XYZ leads. It is equally clear that three-channel simul-

taneous recording would materially simplify this measurement technique and have greater application to investigation of QRS variability in states of physiological stress or disease.

SUMMARY

1. Total QRS duration, from earliest to latest deflections of ventricular activation (depolarization), is not measurable in limb leads, due to isoelectric projection of early or late parts of the spatial QRS vector loop.

2. The most nearly correct value for QRS duration can be obtained only from simultaneously recorded, orthogonal XYZ lead derivations with high fidelity, high-speed recording and tedious measurement technique.

3. Total QRS duration in XYZ leads was measured in 115 men, aged 20 to 50 years. The range of values was 0.0801 second to 0.1309 second, the mean 0.1010 second, the standard deviation 0.010 second.

4. It is suggested that 0.12 second be the "upper normal limit" of QRS duration in XYZ leads. Fifty-four per cent of the values were over 0.10 second; 18 per cent over 0.11 second; and 3.5 per cent over 0.12 second.

5. V_1 and V_2 are suggested as the single leads in conventional records in which the more nearly correct QRS duration may be most often measured.

6. The QRS duration found in isochronous recordings of Leads I, II, and III was uniformly shorter than that in XYZ leads and did not permit prediction of the spatially correct QRS duration. The range of QRS duration in simultaneous records of Leads I, II, and III was 0.765 to 0.109 second, the mean 0.904 second.

7. Poor correlation of QRS duration with heart rate was found except at the extremes of heart rate where correlation was high.

8. Poor correlation was found between QRS duration and body weight (heart size implied).

9. QRS duration increased slightly after exercise in the face of accelerated heart rate.

10. Mean beat-to-beat change in total QRS duration from XYZ leads was on the order of 3 msec., while beat-to-beat change in single lead strips averaged 2 msec.

11. Separation of all positional and other factors in beat-to-beat variability of QRS duration awaits similar measurement in three-channel simultaneous records from apparatus of comparable sensitivity.

12. Subtle beat-to-beat changes, QRS duration change with exercise in normal and abnormal subjects, and "spatially corrected" P-R and Q-T intervals are obviously indicated studies.

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THE EFFECTS OF NONPATHOLOGIC FACTORS ON THE ELECTROCARDIOGRAM

II. Analysis

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WE HAVE presented the observations (as have others)[1-8] that exercise, the taking of food, smoking, and changes in heart rate commonly produce T-wave and RS-T changes which may be similar to those which occur in disease. Since attention was first called to the importance of the effects of such nonpathologic factors in the interpretation of the electrocardiogram, several attempts have been made to establish the limits which these effects may attain in the normal. Our own experience indicates that the empirical criteria suggested in the past are in great part erroneous. We believe that order can be brought to this rather chaotic state of affairs only through the insight which can be furnished by a fundamentally physiologic approach to the study of the recovery (T) potentials.

The QRS potentials are produced by activation or depolarization of the myocardium. The T deflections of the electrocardiogram are produced by the process of recovery. It seems reasonable to assume that recovery must begin in those areas which are first depolarized. Since the sequence of the inception of repolarization is dependent upon the sequence of depolarization, some relationship between the repolarization potentials and the depolarization potentials must exist. Indeed if the *rate* of repolarization were uniform throughout the ventricles, then this relationship would be extremely simple. In Fig. 1*A* we present an oversimplified diagram of a segment of left ventricular wall. Actually, the four "fibers" of the figure represent segments of myocardial syncytium (Fig. 1*B*). The endocardial surface is to the left, the epicardial surface to the right. The point *P* at which the potentials are recorded is assumed to be at such a distance that there is little difference in the solid angles subtended at *P* by the endocardial and epicardial surfaces, respectively. If repolarization begins at the endocardial surface where depolarization began and if the rate of repolarization is uniform throughout the muscle, it is seen that the QRS complex is followed by a T wave which is opposite in direction but equal in area to that of the QRS deflection, for under these circumstances the quantitative net external

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electrical effects of repolarization must be equal and opposite to those of depolarization. It is to be noted that repolarization requires a great deal more time than does depolarization, and, therefore, except at the very beginning and

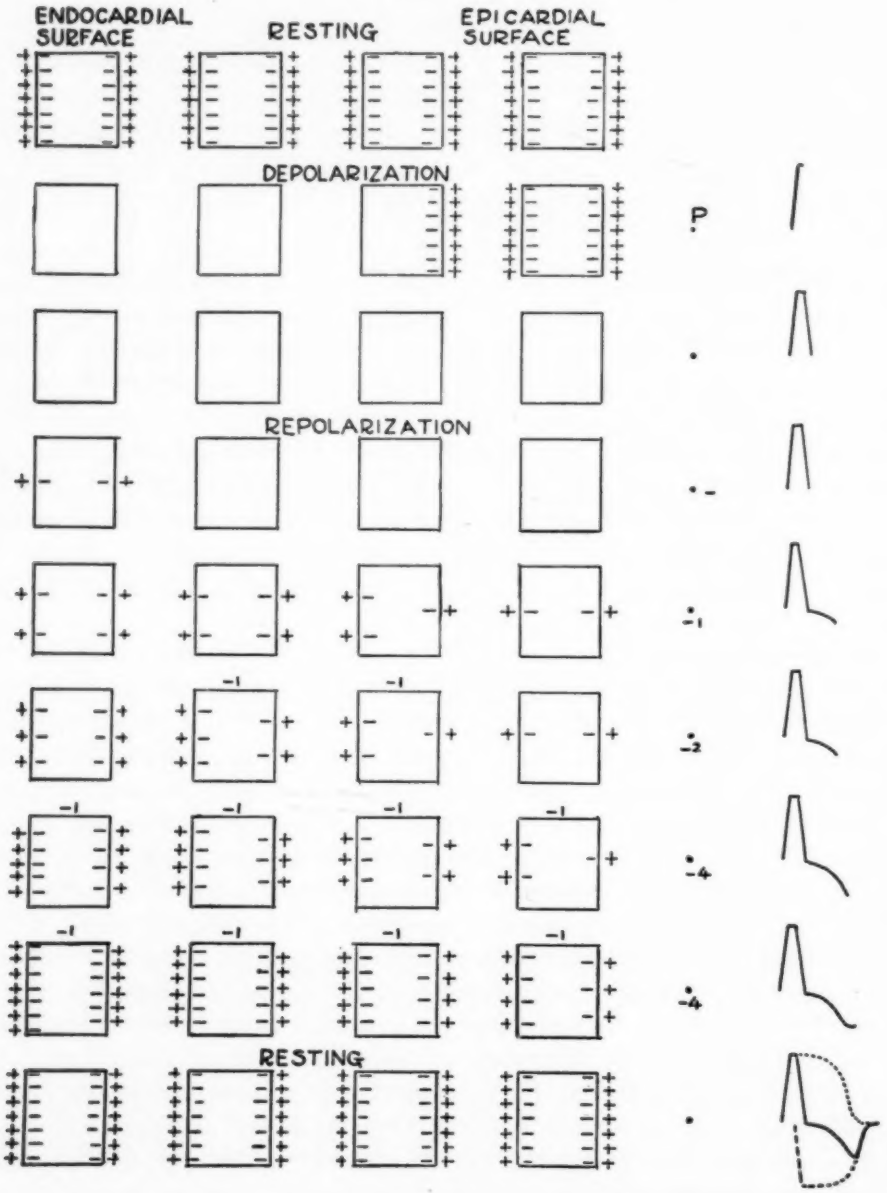

Fig. 1*A*.—A very much simplified representation of a sector of left ventricular wall, here regarded as composed of four fibers. The muscular wall is activated from left (endocardial surface) to right (epicardial surface). The reversal of polarization now known to occur with "depolarization" does not materially effect the results of this presentation. The point *P* is assumed to be at such a distance from the ventricular wall that there is little difference between the solid angles subtended at *P* by the endocardial and epicardial surfaces of the segment of ventricular wall represented. In this figure the time course of repolarization is assumed to be uniform throughout. (For discussion see text.)

at the very end of this process, repolarization is going on simultaneously throughout most of the muscle with the result that opposition of effects occurs. This is in contradistinction to the process of excitation which is very rapid and which may be represented as a wave involving only a limited margin of muscle at any given instant.

It is further to be noted that Fig. 1*A* shows that at any given instant the net effects of the dipoles distributed throughout the muscle are equal to the algebraic sum of the dipole effects of the endocardial and epicardial surfaces. In other words, we need consider only the surface effects. Following Burdon-Sanderson and Page[9] these effects can be represented by monophasic curves. Such curves were recorded experimentally by Ashman and others[13] many years

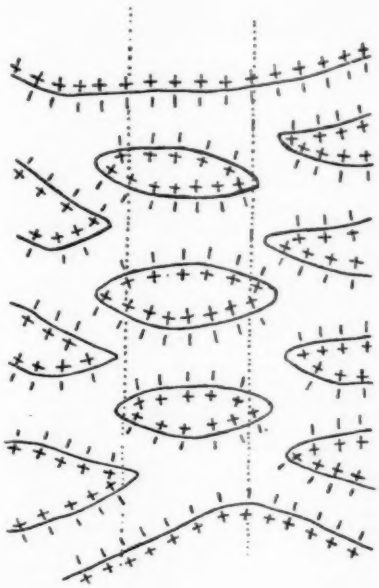

Fig. 1*B*.—The derivation of the simplification of Fig. 1*A*.

ago. Thus, the diphasic curve of Fig. 1*A* may be represented as the algebraic sum of two oppositely directed monophasic curves, one representing the depolarization and repolarization of the endocardial surface and the other the same processes occurring at the epicardial surface (Fig. 2). The algebraic addition of two monophasic curves may be seen in Fig. 3. If the rate of repolarization or "duration of the excitatory state" (Wilson[10]) is uniform throughout the muscle then the diphasic curve representing the net effect will have the form shown in Fig. 1*A*.

Of course, in the human heart when the QRS is upright the T wave is not inverted but is generally upright. It is inferred that this means that the rate of repolarization (or duration of the excitatory state) is not uniform throughout the ventricular muscle. The simplest possible assumption which can be made

to explain the upright T waves is that the rate of repolarization is more rapid at the epicardial surface (Wilson). This is diagrammed in Fig. 4 and as shown in that figure this state of affairs can be represented simply by shortening the duration of the monophasic curve which represents the depolarization and repolarization of the epicardial surface.

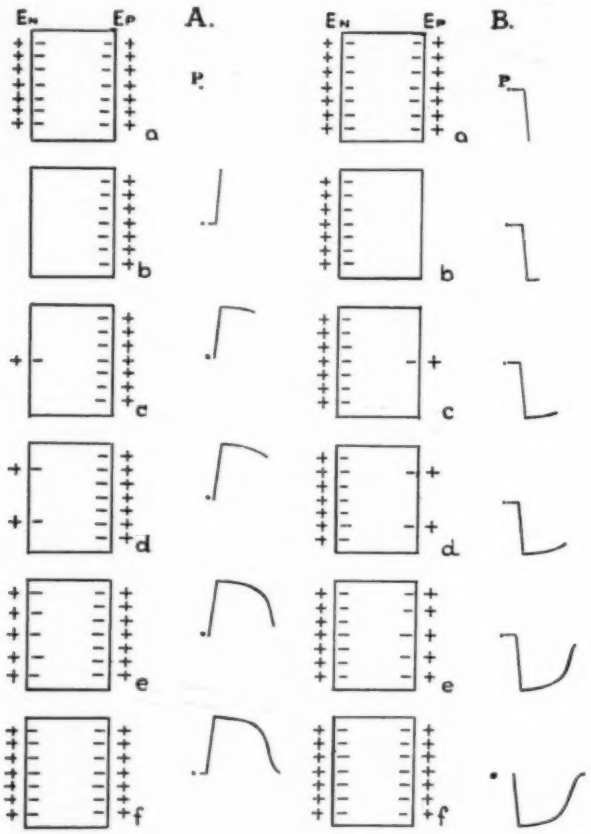

Fig. 2.—Since the net (electrical) effects are derived from a balance between the electrical effects at the endocardial and epicardial surfaces, the left ventricular wall is represented in this figure as a single mass of muscle.

If the epicardial layers of muscle are cooled to the extent that the impulse is blocked before it reaches this surface, then the electrode at *P* will record the deflections produced by the depolarization and repolarization of the endocardial surface when a stimulus is applied (*A*). If, on the other hand, the endocardial layers of muscle are cooled to the same extent, the electrode will record the deflections produced at *P* which result from depolarization and repolarization of the epicardial surface (*B*). The epicardial monophasic curve is simply the inverse of the endocardial monophasic curve if the time course of repolarization is the same at the two surfaces.

Attention is now recalled to the fact that in Fig. 1*A*, where uniform rate of repolarization is assumed, the area of QRS is equal to the area of T and that since T is negative and QRS is positive the area of QRS (AQRS) plus the area of T (AT) equals zero. On the other hand, in Fig. 4 where the rate of repolari-

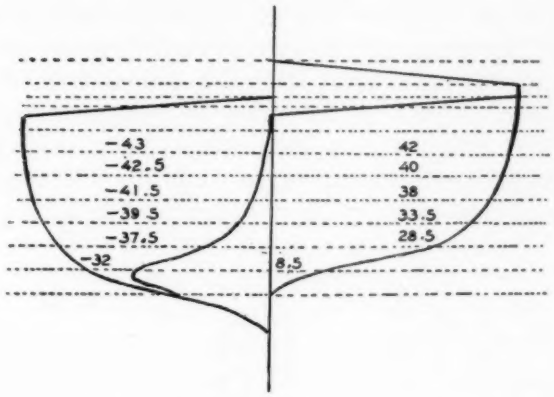

Fig. 3.—If the two monophasic curves are drawn in proper relationship in time, assuming that the endocardial surface is activated first, the biphasic curve ordinarily recorded can be derived by adding these two monophasic curves algebraically.

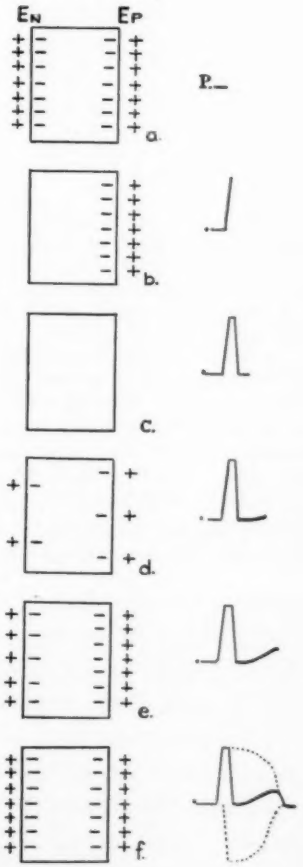

Fig. 4.—A diagrammatic representation of accession and recovery when repolarization is assumed to be more rapid at the epicardial surface.

zation is not uniform the algebraic addition of AQRS and AT results not in zero but in a residuum of some finite value. It seems obvious that this results from the fact that the rate of repolarization is not uniform throughout the muscle and that this quantity, AQRS + AT, may be employed as a measure of the net electrical effect of differences in the rates of repolarization in the various regions of the ventricles or of "local variations in the duration of the excitatory state." It is to this value that Wilson assigned the designation, the ventricular gradient.

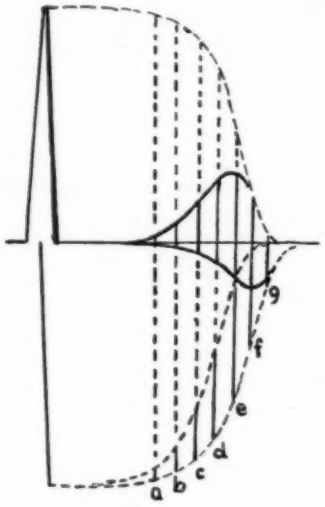

Fig. 5*A*.—The figure shows the two identical but oppositely directed monophasic curves of Fig. 2,*A* and *B* placed in proper time relationship (endocardial monophasic curve first) and added algebraically. The biphasic QRS-T curve with inverted T wave results. If the duration of the epicardial monophasic curve is shortened, algebraic addition of the two curves results in the upright T wave.

The vertical time lines *a*, *b*, *c*, *d*, *e*, *f*, and *g* are employed to add the portions of the monophasic curves which result in the T wave. It is seen that the solid portions of *a*, *b*, *c*, *d*, *e*, *f*, and *g* between the inverted and upright T waves are identical to the solid portions of the same lines between the two monophasic curves. Thus the area enclosed between the two T waves is identical with the difference between the areas of the two monophasic curves. It is this quantity which Wilson called the gradient, the net electrical effect of differences in rates of repolarization.

$$\text{Thus } AT_R + AT = G \text{ (gradient).}$$
$$\text{Since } AT_R = AQRS \text{ (Fig. 1) above.}$$
$$G = AQRS + AT.$$

It is to be noted that the solid lengths of *a*, *b*, *c*, *d*, *e*, *f*, and *g* are instantaneous gradient potentials. The figure makes it clear that these cannot be measured since the regression T wave, T_R, cannot be recorded.

The T wave which, theoretically, would occur if the rate of repolarization were uniform throughout the ventricles so that its form is entirely dependent upon the process of accession is called the *regression T wave*. The gradient potentials may be regarded as those potentials which must be added to the regression T potentials to produce the observed T wave (Figs. 5*A* and 5*B*). The regression T potentials as shown in Figs. 1*A* and 3 are always opposite in direction to the QRS potentials. The vector representing the gradient potentials must point from the area of slow repolarization (the endocardial surface in the normal) to the area of rapid repolarization (the epicardial surface in the normal).

Fig. 6 shows two series of paired monophasic curves. In series *a* the two monophasic curves of each diagram are identical in form and duration, representing uniform rate of repolarization, and it is seen that no matter how the curves are related with respect to time the algebraic sum of AQRS + AT (the gradient) equals zero. In series *b* the lower ("epicardial") monophasic curve is shorter in duration than the upper ("endocardial") monophasic curve, so that we have different rates of repolarization, and it is seen that no matter how the two curves are related with respect to time the algebraic sum of AQRS + AT (the gradient) is again constant but it is not zero. Thus the net electrical effect of differences in rates of repolarization (the gradient) is independent of the path of excitation, for, as shown in Fig. 6 series *b*, the net quantity AQRS + AT (the gradient component) is constant regardless of which area of myocardium is excited first, and regardless of what time interval occurs between the excitation of the various surfaces.

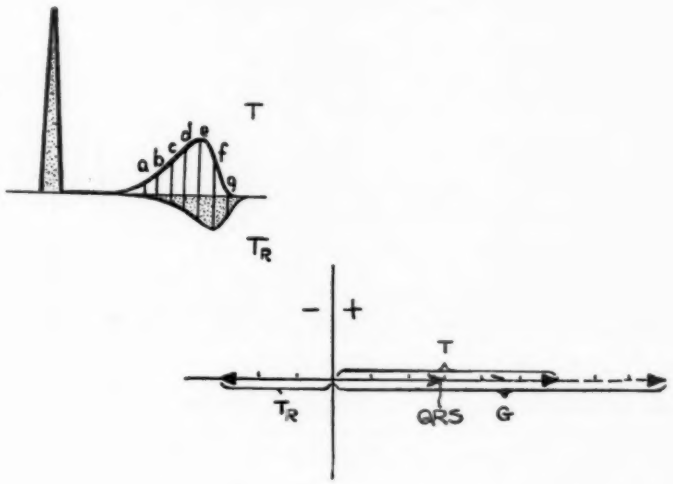

Fig. 5*B*.—The QRS complex and the inverted T wave (T_R) as well as the upright T wave (T) derived in Fig. 2,*C* are shown. T_R is the T wave which results when the time course of repolarization is uniform; it is known as the regression T wave.

The figure is simply a vectorial representation of AQRS, AT_R, AT, and G as they are derived in Figs. 1, 2, and 3. G = T_R + T, T_R = AQRS. Instantaneous G potentials cannot be measured.

Since any lead may be regarded as a component of the summation of a great number of such paired monophasic curves, each representing another segment of ventricular wall, the value AQRS + AT measured in any lead is the component of the ventricular gradient in that lead. It is possible to make important analyses on this basis. For instance, if no change takes place in the rates of repolarization in the various portions of the myocardium so that the gradient remains constant in magnitude and direction, then it will be seen from the expression

$$AQRS + AT = G \text{ (constant)}$$

that if AQRS becomes increased (as in Lead I in left bundle branch block) then

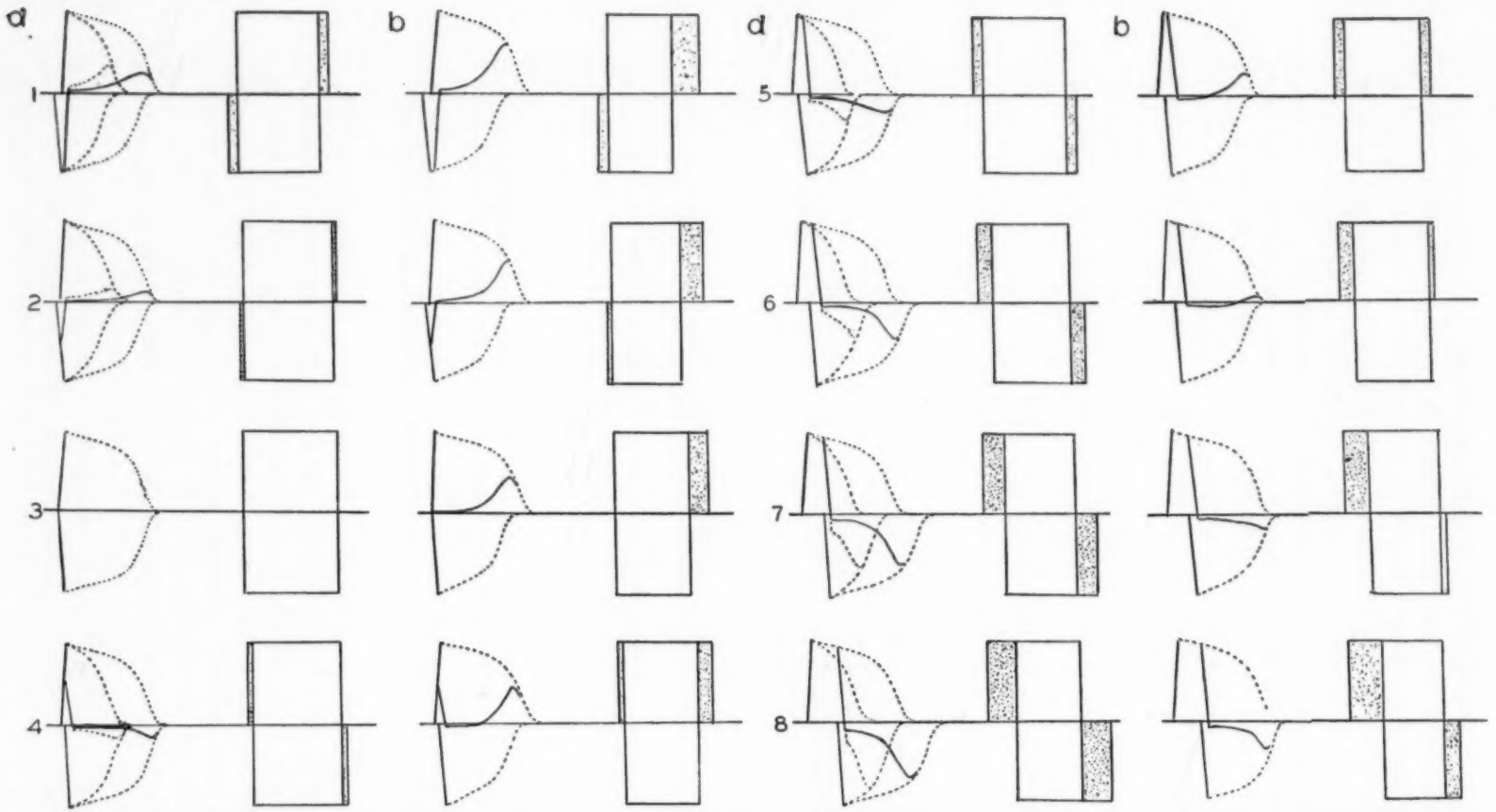

Fig. 6.—*a*, A series of paired monophasic curves of *identical form* but different relationship with respect to time. Each diagram of series *a* shows two pairs of identical monophasic curves, one short and one long. The pairs of identical monophasic curves of series *a* of shorter duration are to be ignored for the moment. It is to be noted as represented in the rectangular counterparts that the algebraic addition of any pair of monophasic curves of series *a* always results in a net value of zero for AQRS + AT.

b, A series of paired monophasic curves which are not identical; the epicardial (lower) monophasic curve is shorter in duration. The relationship of the two monophasic curves in any diagram in series *b* is identical to that of the corresponding diagram of series *a*. It is to be noted that the algebraic addition of the pair of monophasic curves of any diagram of series *b* always gives the same net result for AQRS + AT, but it is not zero. This value is therefore the net result of the difference in the forms of the two monophasic curves (which are constant throughout the series) and it follows that this value (AQRS + AT) may be employed as a measure of the net electrical effect of the difference in the rates of repolarization which the two monophasic curves of different forms are used to represent.

The shorter pairs of monophasic curves of series *a* are applied to the analysis of RS-T segment shifts which occur when the gradient becomes quite small (approaches zero) at rapid rates and with digitalis, the two conditions in which the Q-T intervals become quite short. It is to be noted that in any diagram the RS-T shift is opposite in direction and proportional in magnitude to the area of the QRS complex (as pointed out by Ashman). The shift is dependent upon (1) the relative loss of the plateau of the monophasic curve and (2) the time relationship of the two monophasic curves. We have preferred to assume that the slope of the rapid portion of the monophasic curve under nonpathologic conditions remains unchanged, for Ashman and also Brooks et al. found that it did not change significantly with rate change even when the action potential monophasic curve shortened greatly with rapid rate. Brooks et al. found the slope was more gradual, but began earlier.

AT must become diminished under the conditions postulated. On the other hand, if AQRS is diminished (as when in Lead III an S becomes larger and broader in left bundle branch block) then AT must perforce become larger (Fig. 7). This is the reciprocal relationship which has been called a "negative relationship" by some writers.[12] It is commonly observed in tracings showing varying degrees of left bundle branch block from beat to beat (Fig. 7) and is best proved quantitatively in the Wolff-Parkinson-White syndrome where no disease complicates the picture. It is less perfect quantitatively in ventricular premature beats because the motion of the heart is so different from that with the normal beats and because the length of the preceding cycle affects the magnitude of the gradient.

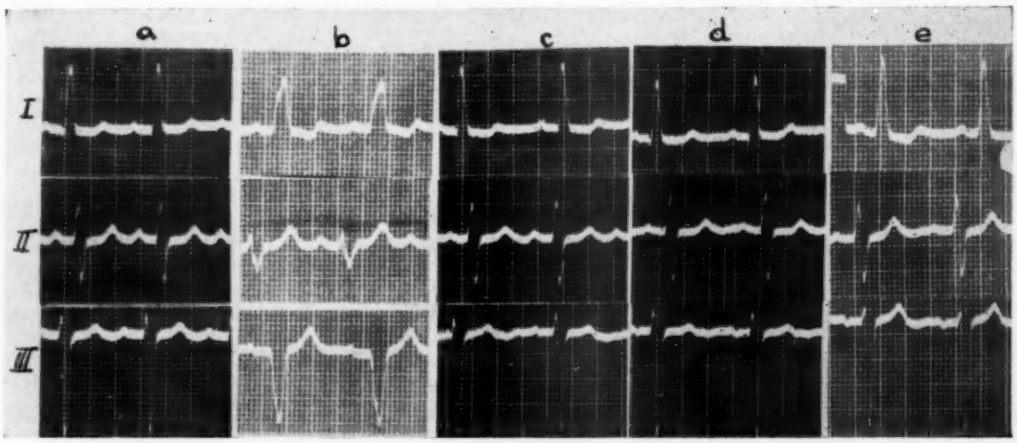

Fig. 7.—A series of tracings from the same patient showing varying degrees of left bundle branch block. Note that in any of the leads the algebraic sum of the areas of the QRS and the area of the T wave tends to remain constant. When the area of QRS in Lead I increases, the area of T decreases; when the negative area of S in Lead III becomes greater, the positive area of T increases.

The Effect of Rate Changes on Repolarization.—Ashman[13] working with the turtle heart recorded monophasic curves with a suction electrode and verified the earlier findings[14,15] that heating increased and cooling decreased the rate of repolarization of the myocardium. Furthermore, he recorded simultaneously monophasic curves from a cooled region and an uncooled region of the same heart. When the heart was artifically stimulated at increasing rates it was found that both the monophasic curve of prolonged duration from the cooled area and the shorter monophasic curve from the uncooled area became shorter with increased rate. He further noted that the longer monophasic curve (from the cooled area) was shortened more than the shorter monophasic curve (from the uncooled area). As the rate was made very rapid, the two monophasic curves approached the same form and duration (see Fig. 8). In other words, the rate of repolarization became more uniform; the gradient between the two diminished. Conversely, when the rate was slowed, the monophasic curves returned to their original forms; the gradient again increased.

It seems reasonable to suppose that we may assume that the same phenomenon observed by Ashman might apply to the various regions of the human heart whose monophasic curves (rates of repolarization) are not uniform. Thus if in Fig. 8 the two monophasic curves approach the same form, i.e., as the gradient diminishes, with increased rate the T wave would be expected to become lower and lower and finally become inverted.[16] Of course the QT interval diminishes at the same time. As the rate becomes slower the reverse changes

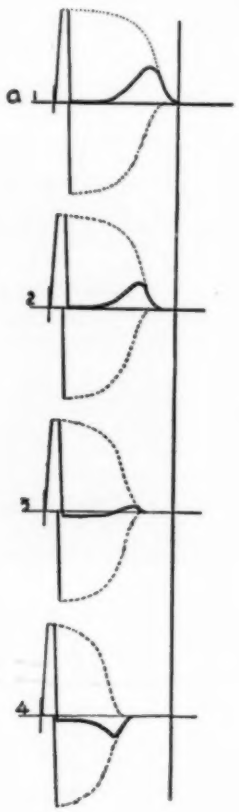

Fig. 8.—The effect of increasing rate upon two monophasic curves of different durations. Here the two monophasic curves are drawn to represent opposing effects (Burdon-Sanderson) so that the figure also includes the expected effect of rate upon the biphasic curves usually recorded in clinical electrocardiography. (For further discussion see text.) (Courtesy Paul B. Hoeber, Inc.)

occur. In serial studies, if the cardiac position does not change so that the mean QRS remains the same, each lead can be analyzed by the two monophasic-curve method employing the principles outlined above and the knowledge that increased rate and other factors (food, exercise, smoking, and digitalis) diminish the magnitude of the gradient but do not alter its direction. This method of analysis permits us to understand why the T waves in perfectly normal persons behave in the manner shown in Figs. 9 and 10. It is to be remembered that if in any lead the QRS is represented largely by a deep S wave, the monophasic

curves of Fig. 8, must be inverted for purposes of analysis. In such leads the component of the gradient in the lead is negative so that when increased rate diminishes the magnitude of the gradient, the component becomes diminished; AQRS + AT then becomes less negative or more positive. T in such instances becomes higher. This may be clearer from the discussion of spatial analysis to follow. Of course, leads with both large R and large S waves cannot be represented by a single pair of monophasic curves; each element of the QRS complex must be represented by another pair of such curves.

Thus, in any lead in which the QRS complex consists largely of an R wave, (Lead I in counterclockwise transverse hearts, Leads II and III in clockwise hearts, and Leads V_4, V_5, and V_6 in all but apex-back hearts), progressive increase in rate, which diminishes the gradient, may be expected to cause a progressive change in the T wave as diagrammed in Fig. 8. Inversion of the T wave and/or RS-T segment depression as shown in the final diagram of Fig. 8 may be expected to occur in all of these leads in perfectly normal hearts as an effect of rapid rate and other factors which diminish the magnitude of the ventricular gradient without altering its direction (Figs. 9 and 10). Conversely, in those leads in which the QRS complex is represented largely by an S wave (Lead III in counterclockwise hearts, Lead V_1 and at times Leads V_2 and V_3), the RS-T segment is elevated and the T wave becomes larger under the same circumstances. Finally, when the QRS complex in any lead is represented by an R and an S, both of important magnitude, the direction of the RS-T and/or T-wave changes will tend to be opposite to that of the deflection (R or S) of the largest area. We have found that the effects of food, exercise, hyperventilation, and of smoking upon the RS-T segments and T waves of the electrocardiogram like the effects of rate increase are due to diminution of the magnitude of the gradient. Frequently the increase in rate which follows exercise, food, and smoking may adequately account for the effects noted. However, the effects frequently persist after the rate has returned to the control level and they also frequently occur without significant rate change.

It is important to emphasize, however, that single lead analysis has sharp limitations. The single lead can reflect only a decrease or an increase in the magnitude of the component of the gradient in that lead. Change in direction of the gradient can be detected only if two or more leads are employed for vector construction as will be outlined under "spatial analysis." This is emphasized here because decided changes in the spatial direction of the gradient in relation to the spatial direction of the mean QRS vector occur only in disease. Furthermore, as presented here, the analysis is dependent upon the validity of single dipole representation which appears to be grossly erroneous for potentials recorded at points very close to the heart, so that the T waves in Leads V_1, V_2, and V_3 frequently behave in a paradoxical manner, becoming inverted (especially with hyperventilation or digitalis) even when the QRS complex in these leads is represented largely by an S wave. This subject will be pursued in a later paper.

The foregoing discussion should make it quite clear that interpretation of T waves without relation to the QRS complex is meaningless.

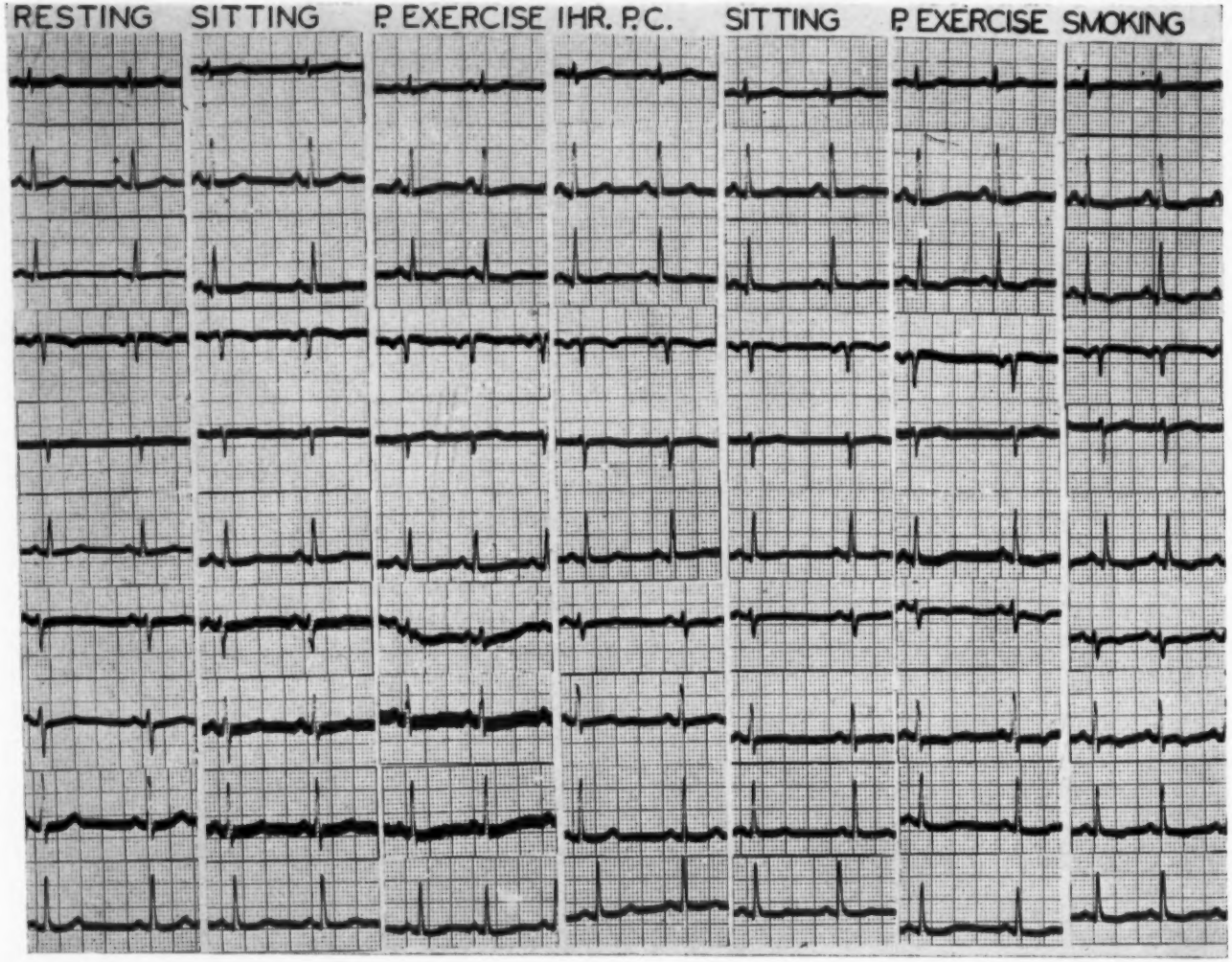

Fig. 9.—Electrocardiograms made on the same individual under the circumstances indicated and in the sequence shown. Note that in every lead in which the QRS complex is represented largely by an R wave, the T-wave changes as a result of exercise and of smoking correspond to those diagrammed in Fig. 8. In this perfectly healthy 21-year-old woman the T waves of every lead except Leads I and V_1 become inverted. In aV_R the T wave was previously inverted and became flat and then upright (smoking) corresponding to the diagrams of Fig. 8 if the latter are inverted so that the QRS complex corresponds.

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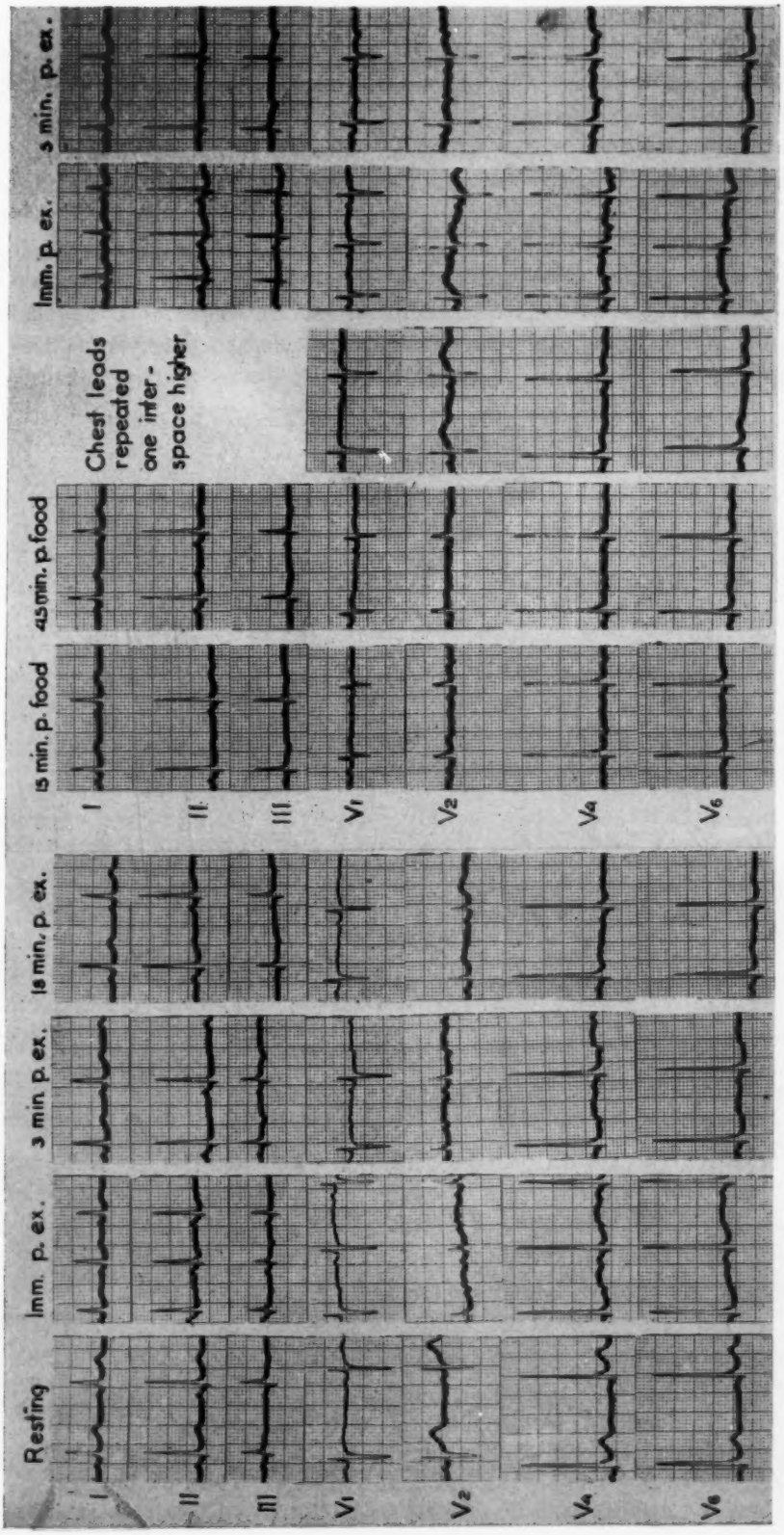

Fig. 10.—A series of observations on the same 21-year-old healthy student nurse. Note changes in T waves in Leads V_4 and V_6 (with exercise after food).

SPATIAL ANALYSIS

Since the area AQRS + AT may be regarded as the component of the gradient in any lead, this value may be measured in any two limb leads and plotted on the Einthoven triangle as a vector quantity. If the quantities AQRS and AT are plotted independently in the same manner, we arrive at the mean frontal plane QRS vector and mean frontal plane T vector, respectively. The frontal plane gradient vector will be found to be the resultant of the vectorial addition of the mean QRS and mean T vectors according to the parallelogram law, Fig. 14. Furthermore, these frontal plane vectors may be regarded as components of corresponding spatial vectors. As shown in Fig. 12, Ashman, Gardberg, and Byer[17] estimated that the mean spatial QRS vector lies at a spatial angle of about 90 degrees to the longitudinal axis of rotation and that

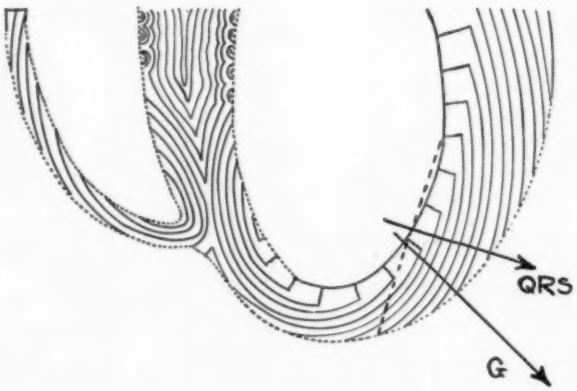

Fig. 11.—Diagram of the successive waves of excitation of the Gardberg-Ashman hypothesis as modified from the original paper. Note that the wave of excitation is visualized as passing diagonally across the left ventricular wall from endocardial to epicardial surface, while the gradient points more perpendicularly across the ventricular wall if the epicardial fibers repolarize more rapidly (or earlier after activation) than the endocardial fibers.

the spatial gradient vector lies in approximately the same plane as these two and at a spatial angle of approximately 30 degrees with the mean QRS vector, and 60 degrees with the longitudinal axis. This angle between the gradient and the mean QRS requires some discussion.

Up to this point the oversimplified diagrams employed show all QRS effects, T effects, and gradient effects lying on the same line; and the mean QRS, T, and gradient values for the conditions diagrammed must also lie on the same line (Fig. 5*B*). However, in the human heart, as shown in Fig. 11, the wave of excitation passes diagonally through the ventricular wall rather than straight across as shown in Figs. 1*A*, 2, and 4. On the other hand, the postulated gradient effects, resulting from differences in epicardial and endocardial rates of repolarization are exerted more or less perpendicularly across the ventricular wall; the ventricular gradient vector points from the areas of slowest repolarization to the areas of rapid repolarization. Thus under the conditions postulated in this discussion, one is not surprised to find the angle between the direction of the mean QRS vector and the gradient vector in the human heart described by Ashman, Gardberg, and Byer.[17]

In Fig. 12 the mean QRS, gradient, and T vectors are depicted in proper relation to the normal QRS loop. The projected shadow of this loop on the Einthoven triangle represents the frontal plane QRS loop. By rotating this loop around its longitudinal, transverse, and anterior-posterior axes, and noting its projection on the various leads on the Einthoven triangle, the limb leads of most normal adults can be reproduced.* Conversely, from the appearance of the extremity leads, one can with practice visualize the frontal plane QRS loop. Although oscilloscopically recorded loops are used in this paper, it should be emphasized that similar loops can be derived from the limb leads of tracings recorded with the electrocardiographic equipment used in clinical practice. The method employed has been described elsewhere.[20]

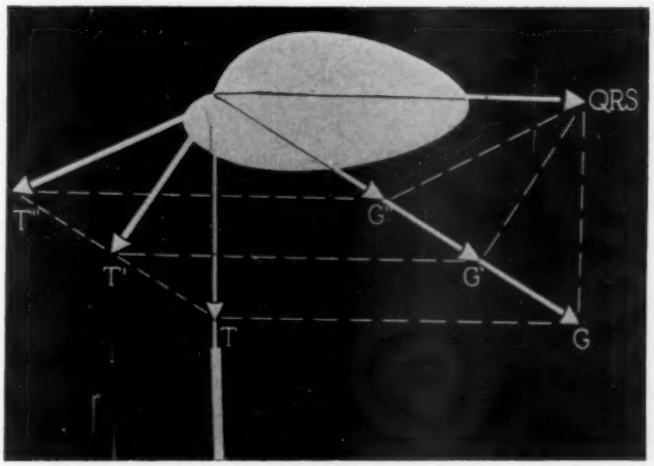

Fig. 12.—The model QRS loop of Ashman and Gardberg, mean spatial QRS vector, spatial gradient vector, spatial T wave vectors, and anatomic axis in their proper spatial relations. T′ results when the gradient is diminished to G′; T″ results when the gradient diminishes to G″. Note that diminution of the magnitude of the gradient without altering its direction increases the spatial angle between the mean QRS and mean T vectors. This photograph was made with the model lying flat on the table. It is not in an anatomic position. (Courtesy New York Academy of Sciences.)

As previously pointed out in the discussion of the analysis of individual leads, changes in the T deflection of the electrocardiogram must be correlated with the QRS deflections and this cannot be accomplished without employing the concept of the gradient. As stated in the previous discussion, Ashman

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***This concept was first proposed by Mann.[18] The loop shown in Fig. 12 was developed from theoretical considerations by Gardberg and Ashman in 1943, and it was later modified to its present shape by Ashman. The constructed or oscilloscopically recorded frontal plane QRS loops of some normal individuals cannot be represented by this idealized loop without certain modifications. To conform to the frontal plane QRS loop of some individuals, this idealized loop must be bent somewhat. It should be pointed out, however, that eccentricity may cause apparent distortions of the recorded frontal plane QRS loop when such do not really exist, and that eccentricity may exaggerate minor distortions of the QRS loop when they do exist. Also in some individuals the mean T-wave vector and gradient vector lie a few degrees out of the plane of the QRS loop. That these slight modifications are necessary is not surprising. They do not detract from the value of using such an idealized loop when considering electrocardiographic problems. Indeed, it would be surprising if any model so simply constructed could illustrate the complicated process of depolarization and repolarization of all normal human ventricles.**

found that the magnitude of the gradient varies with rate. In a subsequent work he showed that digitalis had a similar effect and he predicted that the effect of a variety of nonpathologic conditions would be found to result from changes in the magnitude of the gradient while the direction remained relatively constant.[16,21] Directional changes which do not result from changes in cardiac position are due to disease.

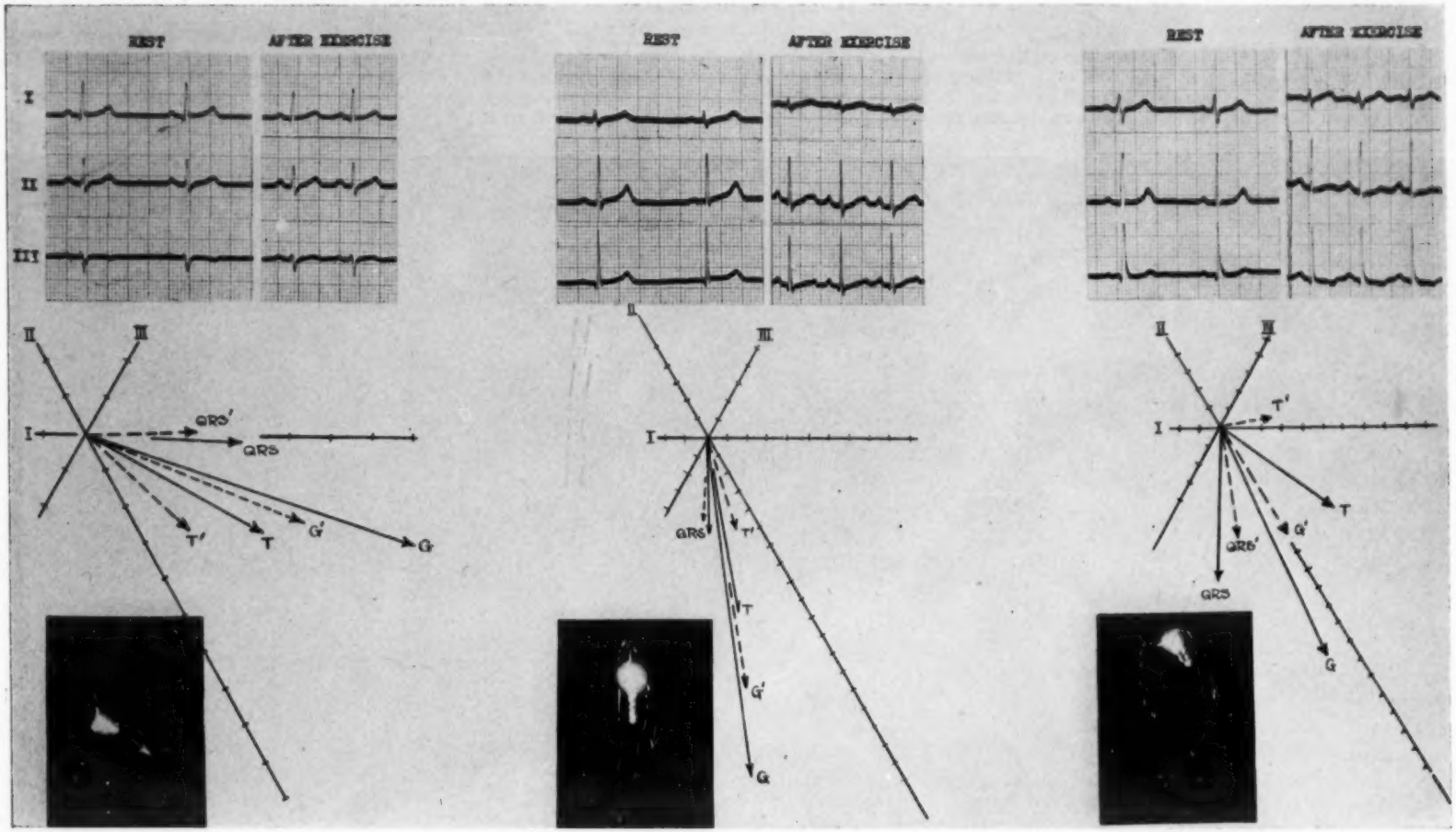
In Fig. 12 it can be seen that when the gradient diminishes in magnitude from G to G′ or G″ the T-wave axis deviates away from the QRS axis (from T to T′ or T″). We now have a loop-vector system which may be employed to represent the limb leads of almost all normal electrocardiograms under a variety of nonpathologic conditions, for Ashman has shown that increased rate, digitalis, etc., simply diminish the magnitude of the gradient without greatly altering its direction.

Fig. 13 shows the same loop in various "anatomical" positions in space. It is noted that when the heart is rotated counterclockwise (Figs. 13,*a* and *b*), the frontal plane gradient lies to the right of the mean QRS, and when the heart is rotated clockwise (Fig. 13,*c*, *d*, and *e*), the gradient lies to the left of the mean QRS. In this figure it is also evident that diminishing the gradient deviates the T-wave vector to the right when a counterclockwise-rotated (electrocardiographic) heart position is present (*a*, *b*), and to the left when a clockwise-rotated position is present (*c*, *d*, *e*). In a nonrotated position the T-wave vector will appear smaller but will not change in direction. Fig. 13,*f* shows the same loop in a slightly more vertical and more apex-forward position. In this instance, marked diminution of the gradient causes T″ to point upward and slightly to the right and, therefore, it predicts, if the analysis holds, that if a subject is found whose loop is in this orientation it should be possible for nonpathologic factors to cause the upright T waves of all three standard limb leads to become inverted.

It can be seen in Fig. 14 that when the mean QRS, mean T, and gradient vectors were plotted, the mean T vector behaved as predicted in Fig. 13. In each case the ventricular gradient was diminished in magnitude by the exercise and, as shown in Fig. 14, this resulted in a deviation of the mean T-wave vector to the right with a counterclockwise heart position (Fig. 14,*A*) and to the left for a clockwise heart position (Fig. 14,*C*). With a nonrotated heart position (Fig. 14,*B*), the mean T-wave vector became smaller but did not change appreciably in direction.

When the empirically alarming T-wave changes of Fig. 14,*D* are viewed in this light, it can be seen that exactly the same change occurred in this individual as in the other normal subjects. Marked diminution of the gradient in an individual with a heart position as was shown in Fig. 13,*f*, will of necessity deviate the mean T-wave vector almost straight upward (Fig. 14,*D*) resulting in a flat or even negative T_I and a deeply inverted T_{II} and T_{III}. This change, therefore, is not pathologic. The reader is reminded that this finding was predicted in the discussion of Fig. 13,*f*. Since the model of the spatial QRS loop, mean spatial QRS, and spatial gradient vector employed in this figure represents the spatial QRS-T relations which prevail in most normal patients, one needs

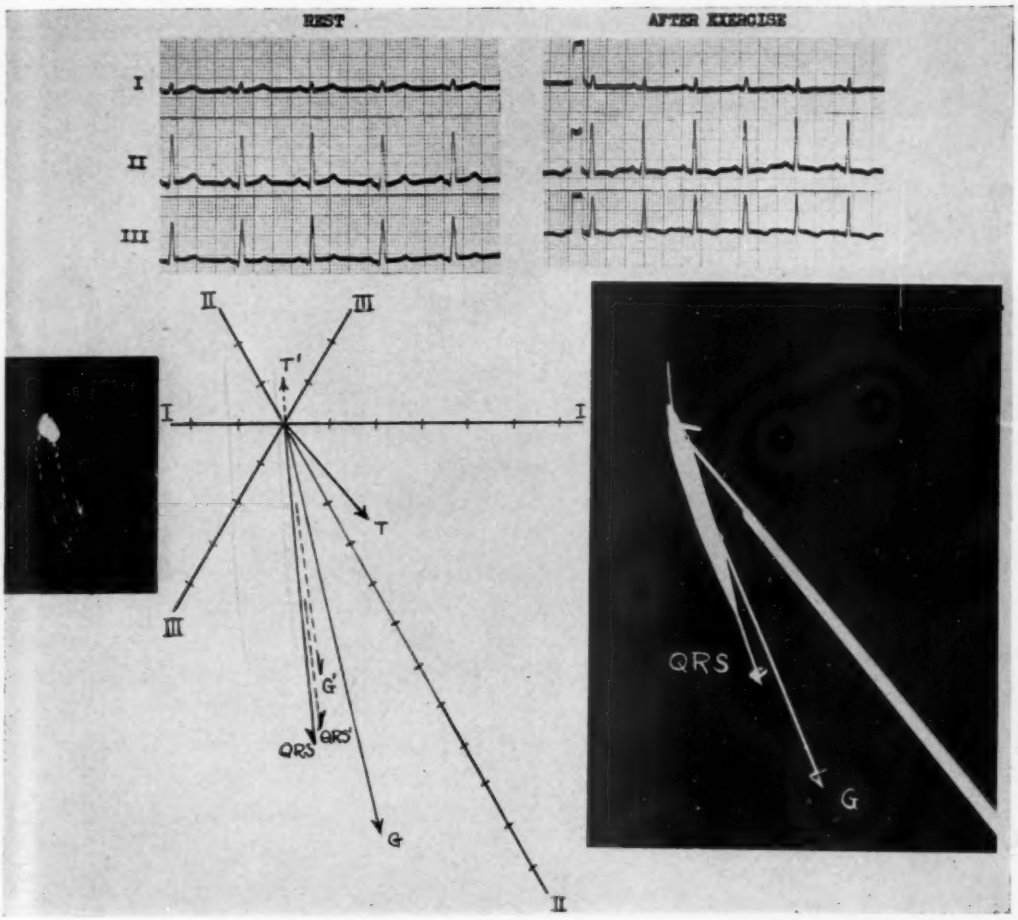
Fig. 13.—Photographs of the model of Fig. 12 in six possible anatomic positions. *a* and *b* represent different degrees of counterclockwise rotation about the anatomic axis (H). *c*, *d*, and *e* represent clockwise rotations. *f* represents clockwise rotation with the apex pulled forward. The projection of the spatial loop and vectors upon the frontal plane (the plane of the photograph) is accomplished by the camera. It is seen that diminution of the magnitude of the gradient causes the T vector to deviate to the right for the counterclockwise rotations and to the left for the clockwise rotations. (Courtesy New York Academy of Sciences.)



A. *B.* *C.*

Fig. 14.—*A* to *C*, Limb lead electrocardiograms, frontal plane vector analysis, and frontal plane oscilloscopic loops of three subjects. Note that in all three subjects the frontal plane ventricular gradient diminished as a result of exercise and that, as predicted in Fig. 13, the T vector deviated to the right in the counterclockwise heart (*A*), and to the left in the clockwise heart (*C*). In the heart in which the loop is viewed almost on edge (*B*) the T vector deviates very little (actually slightly to the left because the loop is not quite on edge). (For further discussion see text.) (Courtesy New York Academy of Sciences.)

only to find the spatial orientation of the model QRS loop whose projection upon the frontal plane corresponds to the QRS complexes of the subject, in order to predict the effects of nonpathologic factors upon the T deflections. Of course, if after exercise or with change in posture, the orientation of the heart and, therefore, of the QRS loop changes (as evidenced by changes in the QRS complexes), the relationship of the projection of the frontal plane gradient axis to the frontal plane mean QRS axis changes (see Fig. 15). By using the model the expected change in the relationship of the gradient to the mean QRS that occurs with



D.

Fig. 14 (Cont'd).—*D*, Limb lead electrocardiograms, frontal plane vector analysis and oscilloscopic loop made on a subject whose cardiac position corresponds to that represented in the photograph of the model in Fig. 13,*f*, reproduced here. Note that the T waves after exercise correspond to the vector *T''* of the photograph of the model as predicted in the discussion of Fig. 13 in the text. (Courtesy New York Academy of Sciences.)

any change in cardiac position can be seen (Fig. 13). When there was a change in the cardiac position after the exercise as revealed by changes in the QRS complexes (and loops), the direction of the gradient changed only to the degree expected from the change in cardiac position (Fig. 15). This subject is dealt

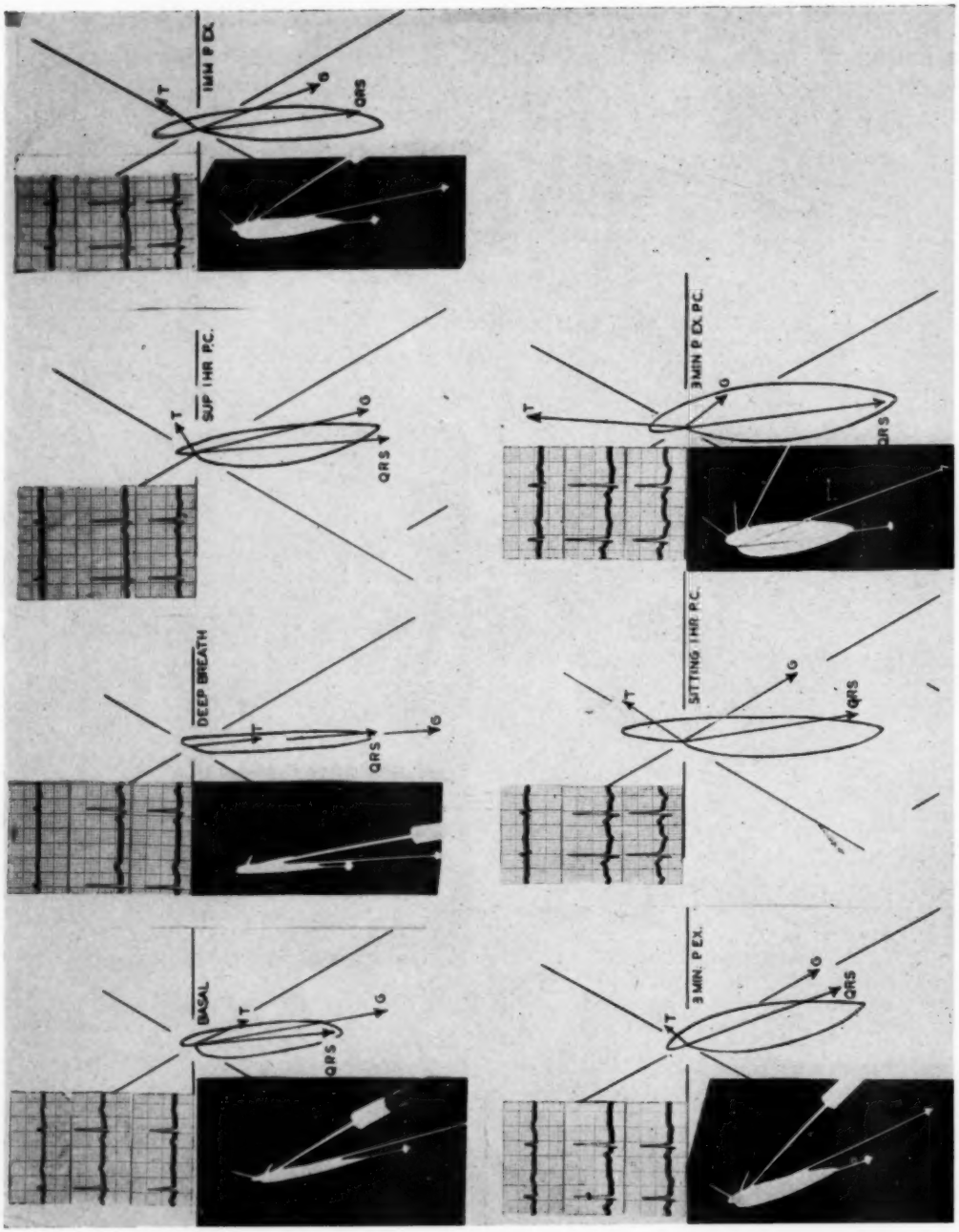


Fig. 15.—A series of limb lead observations made in sequence on the same patient. The loops are drawn from the QRS complexes of the limb leads and the frontal plane. QRS, T, and gradient vectors are plotted. Photographs of the model spatial loop are included which correspond fairly closely to the QRS loop drawn for each observation.

Note (in the photographs) the effect of slight change in the orientation of the spatial loop upon the directions of the frontal plane vectors and the correspondence to the actual observations.

with in more detail elsewhere.[22] The crux of this matter is the spatial relationship of the gradient axis to that of the mean QRS.

Plotting the mean QRS, mean T, and ventricular gradient vectors of our exercise, postprandial and smoking tracings gave similar results. When no change in the cardiac position (i.e., no QRS changes) occurred between observations, the RS-T segment and T-wave changes resulting from these factors were found as predicted by Ashman to be due to a diminution of the ventricular gradient without any significant change in its direction.

It should be noted here that in apex-back hearts the spatial gradient vector may be directed very much backward so that its projection on the frontal plane is small. In such subjects the effect (on the limb leads) of those factors which simply diminish the magnitude of the gradient is much less than in the examples presented here. This subject is dealt with in more detail in another work.[23]

Thus it is seen that the considerable changes which are observed in the T deflections in perfectly normal hearts as a result of exercise, the taking of food, and smoking can be understood only in terms of a physiologic approach embracing an understanding of the ventricular gradient and the factors which influence it. While the foregoing vector approach applies only to the limb leads, the precordial leads (and the limb leads) may be analyzed individually by the two monophasic-curve method illustrated in Fig. 8. It is thus seen that in the precordial leads of the accompanying Figs. 9 and 10 the change in the T deflections result from diminution of the magnitude of the gradient in each lead. It is apparent from a study of Figs. 9 and 10 that as a result of a combination of nonpathologic factors the ventricular gradient can diminish to the extent that inversion of the T waves in nearly all leads of the electrocardiogram results.

Under these circumstances the empirical notion that simple inversion of T waves (without further qualification) in any lead or leads of the electrocardiogram is evidence of disease must be discarded. T-wave changes must be evaluated in terms of the ventricular gradient and a knowledge of the factors which influence its magnitude and direction.

Some individuals we observed showed predominantly T-wave changes while others showed RS-T segment shifts. It is important to point out that the RS-T segment shifts tend to be proportionate in magnitude and opposite in direction to the main deflection of the QRS complex of the lead in which they occur.

Exercise, as a test for coronary insufficiency, is a valuable clinical procedure but interpretation of exercise tracings must be based upon the physiologic principles presented here rather than on rigid empirical criteria. If the RS-T segment and T-wave changes resulting from exercising a patient are those which might result from diminution of the magnitude of the ventricular gradient without change in its direction, these changes should not be considered to be pathologic. Exercise frequently produces electrocardiographic changes in patients with coronary artery disease which can be explained only by a marked change in the direction of the ventricular gradient or to injury phenomena; these changes are unequivocally pathologic. Exercise may, however, produce a pathologic diminution of the magnitude of the gradient without a change in its direction in an

individual with coronary disease. At present we know of no infallible method of distinguishing such changes from nonpathologic changes. It has been shown in several cases reported here that such empirical criteria for abnormal response to exercise as inversion of the T wave in Leads II, V_4, V_5, and V_6 and the occurrence of RS-T segment shifts of arbitrary magnitude are erroneous. It must be repeated here for emphasis that such RS-T segment and T-wave changes that are the result of a diminution of the ventricular gradient without a change in its direction should not be considered pathologic. Only by this conservatism can one avoid seriously disturbing the equanimity of one's patients and their families by presenting to them an erroneous diagnosis of heart disease.

THE SPATIAL ANGLE BETWEEN THE MEAN SPATIAL QRS AND T VECTORS

Some comment must be made with respect to recent attempts to measure spatial vectors directly by oscilloscopic as well as other techniques, and the attempts that have been made to focus attention upon and to evaluate empirically the spatial angle between the mean QRS and mean T vectors. Ignoring for the moment the errors involved in the methods employed (which are dealt with elsewhere), we call attention to the fact that, as shown theoretically in Fig. 12 and experimentally in Fig. 14, the spatial angle between the mean spatial QRS and the mean spatial T vector is increased in perfectly healthy young persons by exercise and other factors. The extent of widening of this angle may be great with degrees of diminution of the magnitude of the gradient which are easily produced under nonpathologic conditions. The importance of understanding this phenomenon in terms of the approach rendered here is emphasized by the erroneous conclusions reached through lack of such understanding. The widening of this angle observed by Simonson[24] after exercise is a perfectly normal phenomenon and did not result from "ventricular ischemia." It must also be pointed out that with progressive diminution of the gradient (Fig. 12) the T axis must first become smaller and then larger.

The spatial angle between the mean QRS and the mean T axis may be widened by other factors. In Fig. 16 QRS is the mean spatial QRS vector, T_o is the mean spatial T vector, and G is the spatial gradient vector of a normal heart. If the gradient is diminished (as by exercise or increased rate), the gradient becomes G′ and the spatial T vector perforce become $T_{G'}$. The spatial angle between the mean QRS and mean T is widened. On the other hand, if the mean QRS is increased to QRS′ (as in left bundle delay, Wolff-Parkinson-White syndrome, or in left ventricular hypertrophy) and if the gradient remains unchanged (as it frequently does), then the T vector perforce becomes T_{G_2} and the spatial angle between the mean QRS and mean T vector is widened in a manner and extent similar to that caused by diminution of the gradient. Finally, if anterolateral ischemia occurs, the gradient is changed from G to G_2 and the QRS remaining unchanged the T vector becomes T_{G_2}. Again the spatial angle between the mean spatial QRS and mean spatial T vector is widened.

We now have demonstrated that the spatial angle between the mean spatial QRS and mean spatial T axis may be widened in a similar manner in three funda-

mentally different ways. Only the relationship between the magnitude and the direction of the gradient to the magnitude and direction of the mean QRS distinguishes them. The widening of the angle caused by diminution of the gradient without change in its direction and without change in the mean QRS is primary, but not necessarily pathologic, as demonstrated before. Widening of the angle due to increase in the mean QRS and without change in the magnitude or direction of the gradient is secondary; pathologic implications can be attached only to the change in QRS. Widening of the angle due to marked change in the direction of the gradient is primary; it is necessarily pathologic. Interpretation of changes in the spatial angle between the spatial mean QRS and the spatial T vector without employing the concept of the gradient leads to erroneous conclusions.

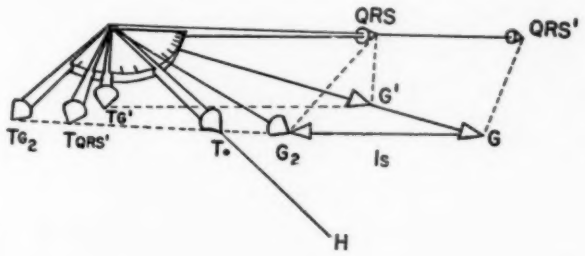


Fig. 16.—The spatial QRS-T angle. *QRS* **is the normal mean spatial QRS,** *G* **is the normal spatial gradient,** T_o **is the normal spatial T vector.** *G'* **is the spatial gradient diminished in magnitude by nonpathologic factors. Since the spatial QRS remains unchanged,** $T_{G'}$ **becomes the mean spatial T vector.** *QRS'* **is the mean spatial QRS for the left ventricular hypertrophy,** *G* **remains the same, and** $T_{QRS'}$ **becomes the mean spatial T.** *Is* **is an ischemic vector due to lateral wall ischemia which changes the direction and magnitude of the spatial gradient vector to** G_2**. If the mean spatial QRS remains unchanged,** T_{G_2} **becomes the mean spatial T vector. Note that under all of the above conditions the spatial angle between the mean spatial QRS and mean spatial T wave is widened in the same fashion. (Courtesy New York Academy of Sciences.)**

SUMMARY AND CONCLUSIONS

Changes in the RS-T segment and T waves of the electrocardiograms of normal persons that result from exercise, the taking of food, and postural change are analyzed employing the ventricular gradient as an instrument.

It was found that RS-T segment shifts and T-wave inversions may occur in almost any lead of the electrocardiograms of normal persons as a result of the nonpathologic factors listed above, and that these effects resulted from diminution of the magnitude of the gradient.

Interpretation of RS-T segment and of T-wave changes without regard to the effects of these factors leads to error. Interpretation of the effects of these factors without employment of the concept of the ventricular gradient is impossible. The same statement applies to interpretation of changes in the spatial angle between the spatial mean QRS and spatial mean T vector.

We wish to acknowledge the help of Dr. Richard Ashman in the preparation of this paper.

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PHONOCARDIOGRAPHIC CHANGES IN MITRAL STENOSIS BEFORE AND AFTER VALVULOTOMY: A CORRELATION WITH MITRAL VALVE SIZE

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VARIATIONS in the phonocardiograms in mitral stenosis have received increasing attention. In addition to the characteristic diastolic murmur, accentuated apical first sound and pulmonary second sound, two other important alterations are frequently found. The first is an increase in the time interval between the onset of the QRS complex of the electrocardiogram and the start of the maximal vibrations of the first heart sound (*"Q-1" interval*).[1-3] The other alteration, almost diagnostic of mitral stenosis, is the occurrence of an opening snap following the second heart sound.[4,5] The time interval between the onset of the second heart sound and the opening snap has been termed the *"2-OS" interval*.[3] (See Fig. 1.)

Variations in the time interval between the initial wave of the electrocardiogram and the onset of the first sound[2,3,8] have been described previously. Wells considered that the maximal vibrations of the first sound complex normally occurred within 0.06 second after the onset of the QRS complex. Prolongation of this interval was found in mitral stenosis.

The opening of stenosed mitral valves frequently produces characteristic vibrations, occurring shortly after the second heart sound and termed the mitral opening snap. Characteristically best recorded at the left sternal border or apex, the opening snap occurs from approximately 0.06 to 0.12 second after the onset of maximal vibrations of the second heart sound. Occasionally a split pulmonary second sound or third heart sound may mimic an opening snap. In those cases, differentiation is aided by a study of a simultaneous apex cardiogram or jugular tracing.

Messer and associates,[6] and Wells[3] studied patients with auricular fibrillation and mitral stenosis. Their findings pointed to a definite relationship between the previous cardiac cycle and the time of opening and closing of the mitral valves. As the previous cycle length increased, the Q-1 interval decreased and the 2-OS interval increased in a linear fashion. Wells found that this linear relationship held true for cycle lengths between 0.6 and 1.2 seconds. It is be-

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TABLE I. SUMMARY OF MEASUREMENTS LISTED IN ORDER OF INCREASING INITIAL VALVE SIZE

PATIENT	BEFORE VALVULOTOMY					AFTER VALVULOTOMY				
	RHYTHM	CORRECTED Q-1 IN SECONDS	CORRECTED 2-OS IN SECONDS	Q-1 MINUS 2-OS	VALVE AREA SQ. CM.	RHYTHM	CORRECTED Q-1 IN SECONDS	CORRECTED 2-OS IN SECONDS	Q-1 MINUS 2-OS	VALVE AREA SQ. CM.
C.C.	Aur. Fib.	.09	.06	3	.15	Aur. Fib.	.08	.08	0	2.1
L.F.	Aur. Fib.	.09	.11	−2	.15	Aur. Fib.	.06	.12	−6	2.9
J.D.	Sinus	.10	.06	4	.15	Sinus	.10	.09	1	2.1
I.M.	Sinus	.09	.07	2	.20	Sinus	.08	.09	−1	2.9
I.W.	Aur. Fib.	.09	.11	−2	.25	Aur. Fib.	.06	.12	−6	3.1
H.M.	Aur. Fib.	.11	.06	5	.30	Sinus	.09	.07	2	2.3
B.C.	Sinus	.09	.06	3	.30	Sinus	.08	.08	0	2.1
M.H.	Sinus	.09	.11	−2	.30	Sinus	.08	.12	−4	3.2
P.A.	Sinus (1° A-V Block)	.10	.06	4	.35	Sinus (1° A-V Block)	.07	.08	−1	2.2
C.O.	Sinus (IV Cond. Def.)	.13	.10	3	.40	Sinus	.10	.08	2	4.0
F.L.	Sinus	.09	No OS	—	.20	Sinus	.06	No OS	—	2.6
C.H.	Sinus (1° A-V Block)	.12	No OS	—	.25	Sinus	.08	No OS	—	2.8
P.W.	Sinus	.09	No OS	—	.30	Sinus	.07	.08	−1	2.8
M.R.	Sinus	.09	.11	−2	.35	Sinus	.08	No OS	—	2.9
S.C.	Sinus	.08	No OS	—	.80	Sinus (1° A-V Block)	.08	No OS	—	3.1
F.A.	Sinus	.08	No OS	—	1.90	Sinus (2° A-V Block)	.05	No OS	—	2.9

lieved that the pressure gradient across the mitral orifice determines the variation in Q-1 and 2-OS intervals.[3,5,6] After a short diastolic interval, left auricular pressure remains high, causing both a delay in closure of the mitral valve and an acceleration in its opening. After a long diastole, greater left ventricular filling occurs, resulting in a more efficient and forceful contraction. This speeds the onset of the first sound and delays the opening snap.

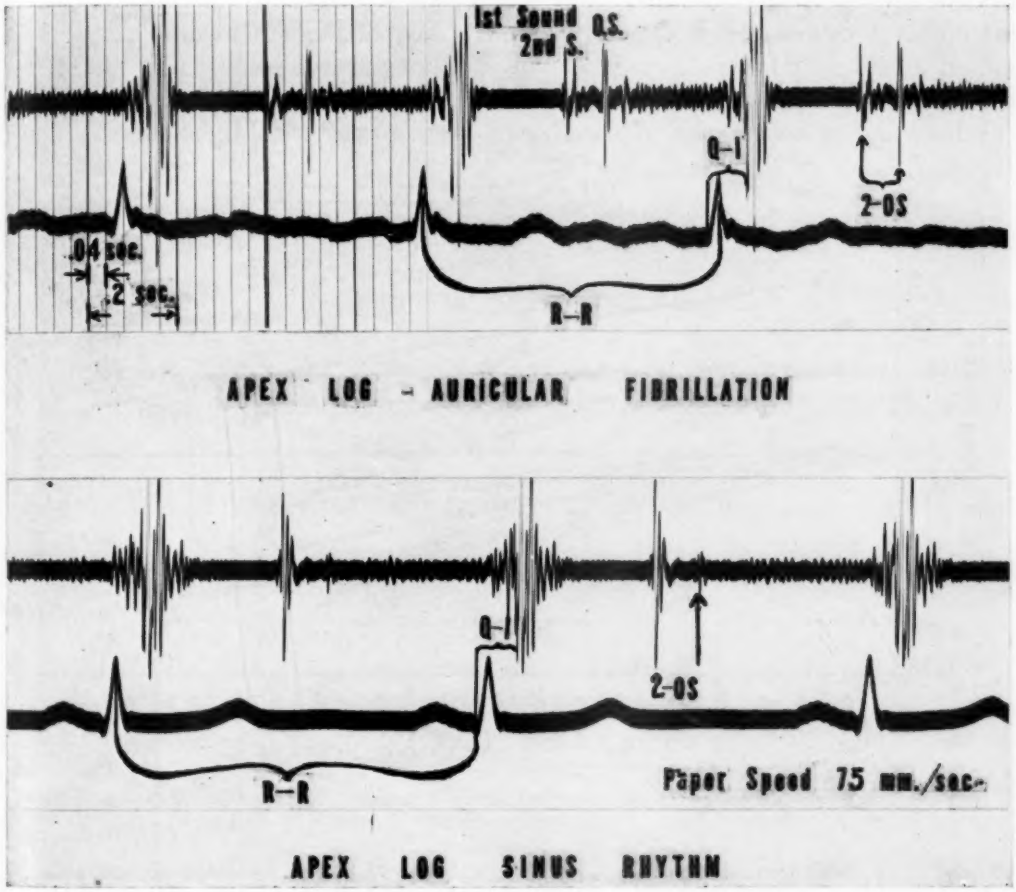

Fig. 1.—Logarithmic phonocardiograms obtained at apex. Tracing above illustrates periods of measurement in auricular fibrillation. Tracing below illustrates measurement in patient with normal sinus rhythm.

Bayer and associates[7] performed cardiac catheterizations on 100 patients with clinical mitral stenosis. Simultaneous pulmonary capillary pressures, phonocardiograms, and systolic brachial blood pressures were taken. The pulmonary capillary pressures were considered to be a "transmitted copy" of the left auricular pressures. Among their findings was the observation that a shortened 2-OS interval indicated elevated left auricular pressure. Following successful valvulotomy, the 2-OS interval lengthened.

Various authors[3,9,10] have been interested in the Q-1, 2-OS, and Q-1 minus 2-OS intervals as a means of estimating the degree of stenosis of the mitral value.

Because of the apparent significance of these phonocardiographic observations, a study was made of a group of patients undergoing mitral valve surgery at the University of Kansas Medical Center.

MATERIAL AND METHODS

Sixteen patients were suitable for the study. All had simultaneous logarithmic phonocardiograms and Lead II electrocardiograms recorded before and after mitral valvulotomy. The approximate size of the mitral orifice was estimated at surgery before and after valvulotomy; the same surgeon made the estimate in each case. The Q-1 and 2-OS intervals, previous cycle length (R-R), rhythm, and abnormalities of conduction were noted with the Sanborn Twin Beam.

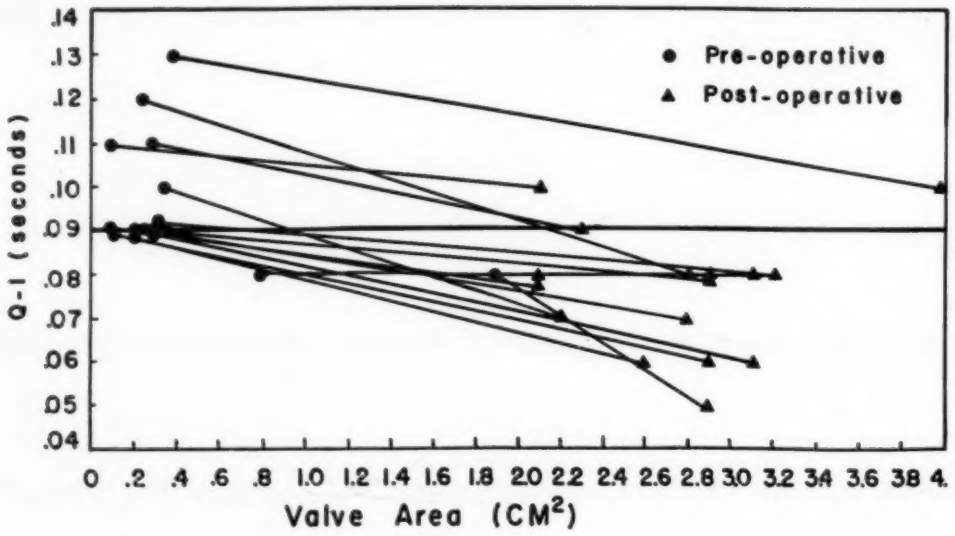

Fig. 2.—This graph illustrates the relationship of the Q-1 interval to the mitral valve area, before and after surgery.

Following Well's method,[3] the Q-1 and 2-OS intervals of the fibrillating patients were corrected to a cycle length of 0.8 second by the use of a scatter graph. Wells noted a variation of 0.03 second in Q-1 and 2-OS intervals between cycle lengths of 0.6 and 1.2 seconds in patients with fibrillation. This finding was utilized in correcting the Q-1 and 2-OS intervals in those patients with sinus rhythm. Although this method is probably not accurate for determining absolute values, it does eliminate the comparison of intervals based on dissimilar rates.

RESULTS

The measurements obtained from 16 patients with mitral stenosis are recorded in Table I.

The Q-1 interval was initially prolonged in all patients (0.08 to 0.13 second).

Following valvulotomy, it decreased in 14 and remained unchanged in 2. One of the latter had a relatively large valve area initially (0.78 cm.^{2}).

In 10 patients, opening snaps were recorded before and after surgery. In 9 of these, the 2-OS interval was increased after valvulotomy. One patient (C.O.)

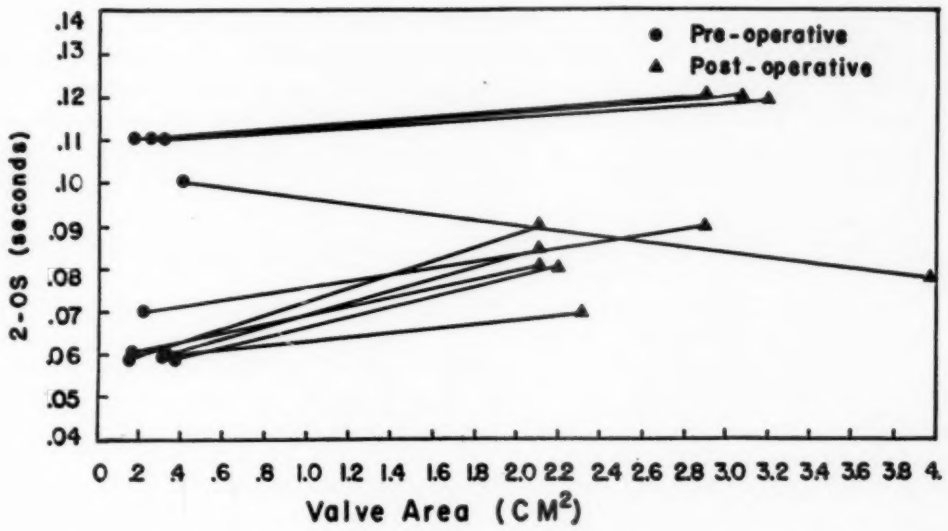

Fig. 3.—This graph illustrates the relationship of the 2-OS interval to the mitral valve area, before and after surgery.

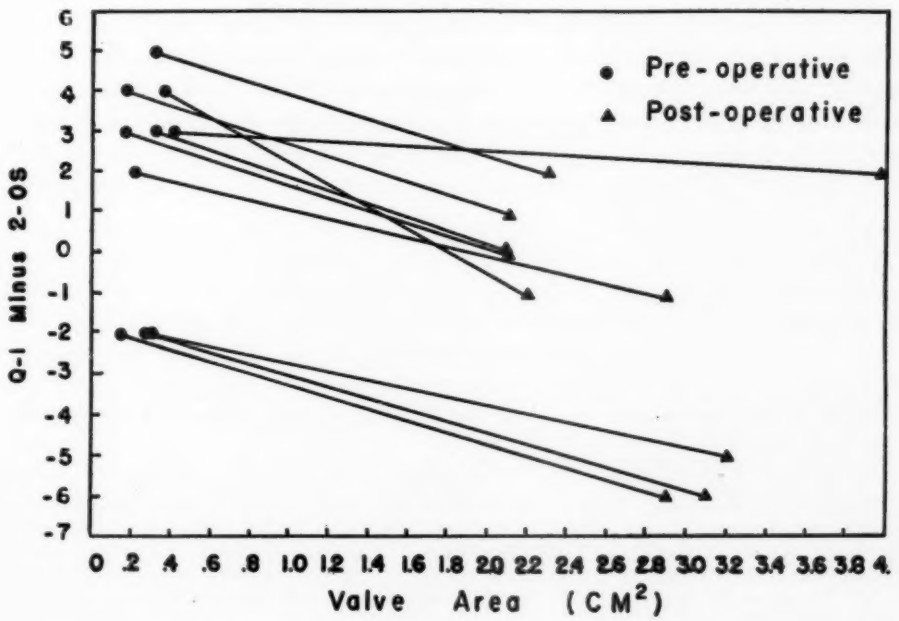

Fig. 4.—This graph illustrates the relationship of the Q-1 interval minus the 2-OS time to the mitral valve area, before and after surgery.

showed a decrease, but was noted to have an intraventricular conduction defect in the preoperative tracing which was not present postoperatively.

The Q-1 minus 2-OS values were determined in these 10 patients, and in each instance became more negative following enlargement of the stenotic valve.

DISCUSSION

On the basis of these data, it is apparent that a prolonged Q-1 and an opening snap are characteristic phonocardiographic findings in mitral stenosis.

When these findings are plotted individually against the valve area, as calculated by the operating surgeon, in order to determine whether they will provide a quantitative index to valve size prior to operation, one finds that there is little or no quantitative correlation (Figs. 2, 3, and 4), although in almost every case opening of the valve was associated with a detectable change in these measurements.

SUMMARY

1. Sixteen patients with mitral stenosis were studied by simultaneous logarithmic phonocardiograms and Lead II electrocardiograms, before and after valvulotomy, in an effort to correlate phonocardiographic measurements with the surgically estimated valve size.

2. An opening snap was present in 10 patients. The 2-OS interval was increased postoperatively in all except one of these.

3. The Q-1 minus 2-OS value uniformly decreased after surgical enlargement of the valve.

4. The Q-1 interval (onset of QRS to maximal vibrations of the first sound) was uniformly prolonged to 0.08 second or more preoperatively. In 14 of the 16 patients, it measured 0.09 second or more. All of these were found at surgery to have tight mitral stenosis with estimated valve areas of 0.4 cm.^{2} or less. After operation, Q-1 was reduced in all except one of these. This same interval in normal patients is 0.06 second or less.[11] This correlation, namely, prolongation of the Q-1 to 0.09 second or more in the presence of very tight mitral stenosis, seems to be a clinically reliable finding.

Ronald L. Linsheid, M.D., and Fethi Gonlubol, M.D., were very helpful in the study of these patients. The authors also are indebted to Dr. C. Frederick Kittle, who performed the surgery and furnished the data on the mitral valve measurements.

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THE PRESSURE EVENTS OF THE CARDIAC CYCLE IN THE DOG: MITRAL VALVE LESIONS

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WHILE valvular lesions produced experimentally in the laboratory can only approximate the hemodynamic conditions of the diseased state in man, they have the distinct advantage of providing a preparation free of superimposed myocardial disease. Numerous investigators have studied the effects of isolated lesions of the mitral valve; and the cardiodynamic changes following experimental mitral insufficiency[1-6] and experimental mitral stenosis[7-10] are well known. However, little work has been reported on the combined lesion of mitral stenosis and insufficiency and the manner in which one lesion alters the effects of the other.

The difficulty in producing and adequately recording simultaneous pressure pulses in a preparation with multiple valvular defects, without incurring a serious degree of congestive failure or shock, has retarded such studies. When multiple, bulky cannulae are inserted into the heart at one time, it is unavoidable that interference with normal myocardial contraction takes place.[11] Care must be taken to avoid confusing the effects of cardiac dilatation and failure with the effects of pure valvular lesions.

The technique of recording 3 pressure curves from the left atrium, left ventricle, and aorta, using manometers adjusted to equal sensitivity[15,16] has not been utilized previously in order to study experimentally produced mitral lesions. Substitution of needle cannulae and strain-gauge manometers, and the use of oscillographic recording instruments has made it possible to record simultaneously 3 equisensitive pressure curves in superimposed fashion. The pressure events of the entire cardiac cycle with multiple valvular lesions can be inscribed graphically in this manner. The following report deals with the experience obtained in 39 dogs studied with this technique, in whom isolated and combined lesions of the mitral valve were created acutely.

METHODS

Adult mongrel dogs, weighing 14 to 28 kilograms, were anesthetized with intravenous Nembutal, 30 mg./Kg. Positive pressure respiration was maintained with 100 per cent oxygen delivered through an endotracheal tube at a cycled pressure of 10 to 15 cm. of water, by means of a pneophore demand valve. Respiration was momentarily suspended while pressure measurements were being recorded.

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*This work was done during Dr. Wilder's tenure as a Fellow of the New York Heart Association.

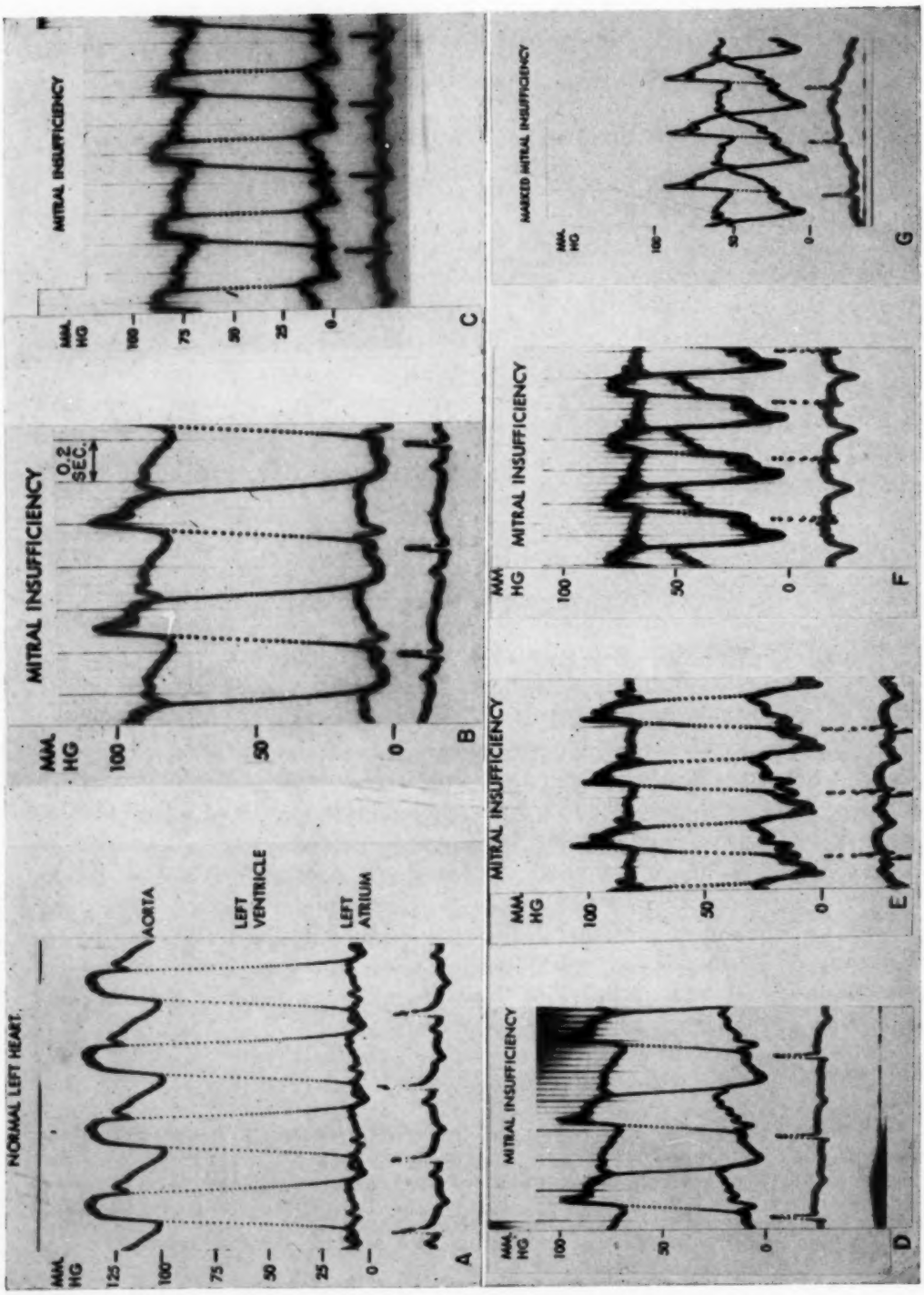


Fig. 1.—The cardiac cycle of the normal left heart of the dog, *A*, and five examples of mitral insufficiency. *B,C,D,E,* and *F* represent different dogs with mitral valve lesions ranging from slight to massive regurgitation. In this and all other figures the interval between the heavy vertical time lines is 0.2 sec., as shown in *B*.

The thorax was entered through the fourth left intercostal space. The pericardium was opened widely and sutured to the chest wall to form a loose cradle support. Vagus nerves were left intact. Mitral insufficiency was produced in 17 dogs by passing a nerve hook through the left ventricular wall and tearing part of the posterior mitral valve leaflet and/or chordae tendineae. The nerve hook was guided to its proper position by the operator's finger in the left atrium. In addition, insufficient orifices of known diameter were simulated by inserting a graduated series of thin-walled brass tubes, attached to 20-gauge needles, into the mitral ring through the left atrial appendage. In this way the degree of regurgitation could be controlled while pressures were recorded. Mitral stenosis was created in 14 dogs by passing a circumferential suture of heavy, braided silk and tightening it at the level of the mitral annulus, above or

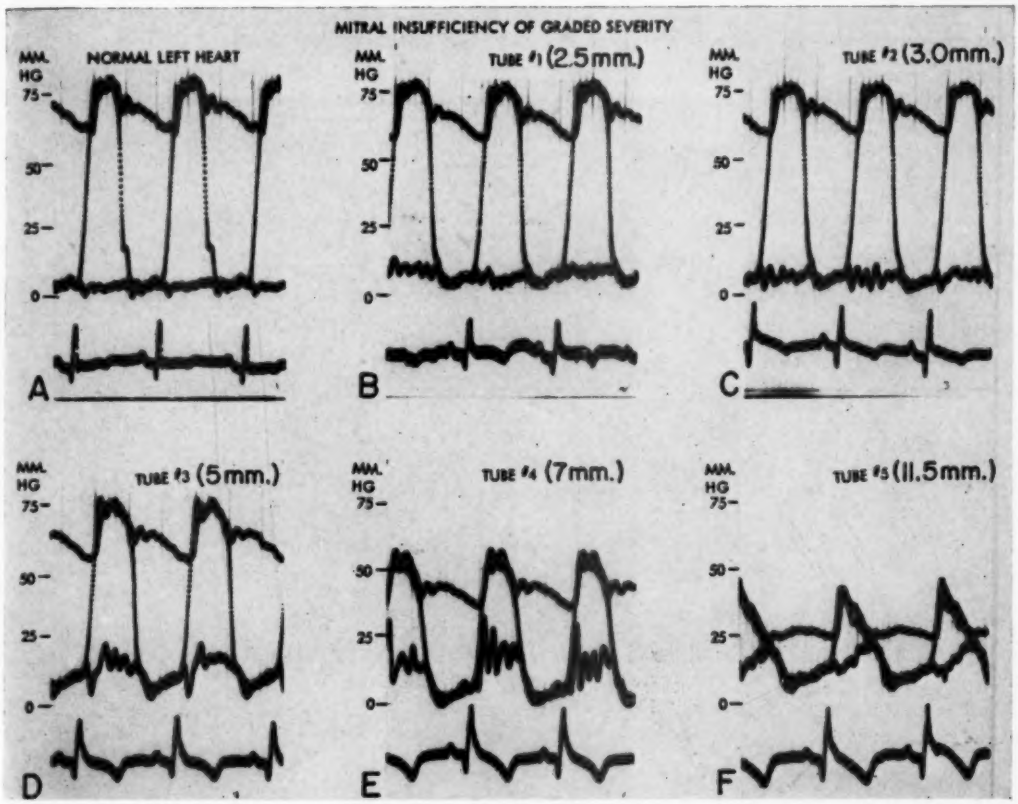


Fig. 2.—Mitral insufficiency. Progressively increasing mitral insufficiency in the same dog produced by inserting graduated tubes into the mitral orifice. The inside diameter of the tubes varied from 2.5 to 11.5 mm. Note that significant pressure changes begin with an insufficient orifice of 5 mm. Despite the development of major regurgitation, the slope of the isometric contraction phase of the left ventricle does not change appreciably until shock and failure ensue (*F*).

below the circumflex coronary artery. The suture was passed through the potential space between the two atria and anchored in the interatrial septum, utilizing a modification of the technique of Sondergaard.[12] In 8 dogs, the combined lesion of mitral stenosis and insufficiency was produced. Whole-blood transfusions were given routinely in order to counteract the loss of blood during operative procedures.

The cardiac chambers were pierced with 18-or 20-gauge needles, 1½ inches long, attached to 4-foot lengths of nondistensible vinyl tubing, with an inside diameter of 1.9 mm. The pressures were led into 3 matched Stathem P23A strain gauges. Pressure tracings were recorded on a

different dogs with mitral valve lesions ranging from slight to massive regurgitation. In this and all other figures the interval between the heavy vertical time lines is 0.2 sec., as shown in *B*.

4-beam oscillograph, which permitted the simultaneous inscription of pressure pulses from the left atrium, left ventricle, and aorta, together with an electrocardiographic lead. A simple adjustment made it possible to record the 3 curves from identical zero lines at equivalent sensitivities. Paper speed was 50 mm./sec. Time lines permitted measurements to the nearest 0.01 sec.

RESULTS

1. *Mitral Insufficiency.*—Examples of the pressure pulses of the cardiac cycle of the left heart in dogs with experimentally produced acute mitral insufficiency of various degrees are shown in Fig. 1. An example of the pathologic lesion created in one of the dogs is illustrated in Fig. 3. Frequently, the chordae tendineae of the posterior mitral leaflet were torn, as well as the leaflet itself.

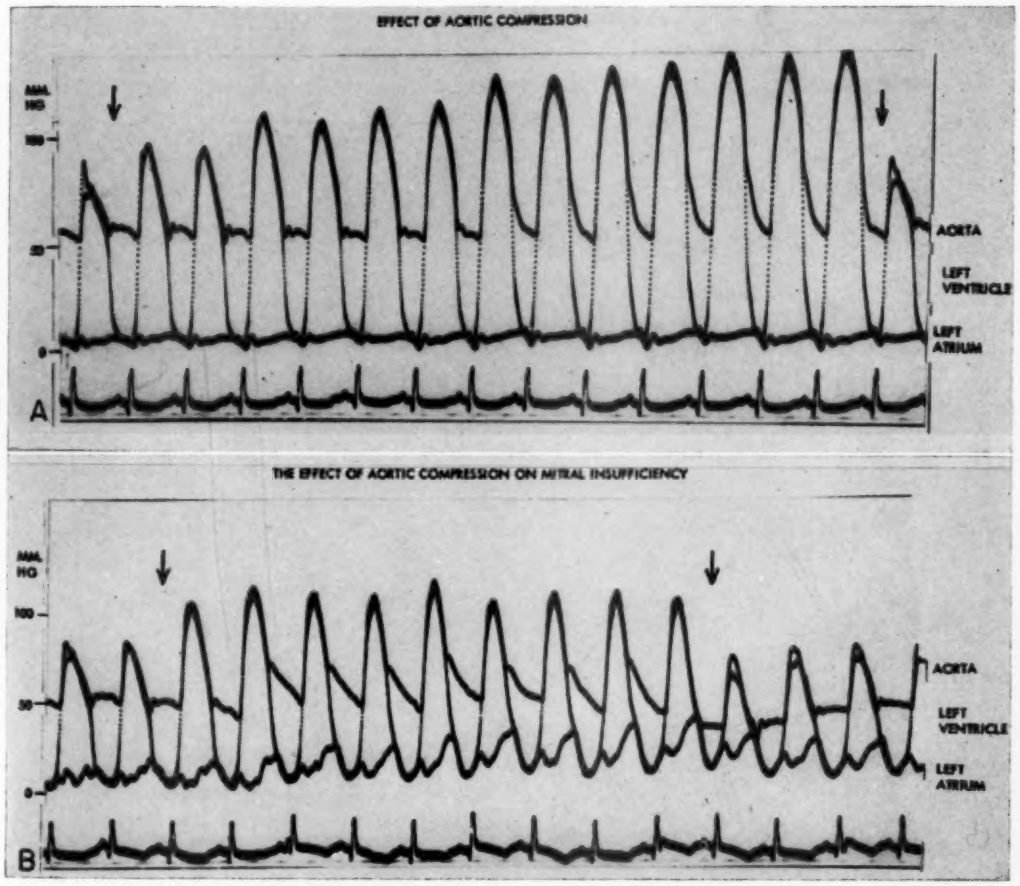
Fig. 3.—Mitral insufficiency. Close-up view of posterior leaflet of mitral valve showing one example of the lesion produced by the nerve hook.

Alterations in the contour of the pressure pulses of the left heart varied directly with the volume of the mitral reflux produced. The earliest change noted was accentuation of the late systolic *v* wave of the left atrial curve. Insufficiency of moderate degree produced progressive loss of the descent of the base (*x* descent) following the atrial *c* wave, and the *v* wave began its ascent sooner and rose to higher levels during late systole and early diastole. Insufficiencies of this degree often resulted in fusion of the atrial *c* and *v* waves. Vibrations corresponding to the apical systolic murmur could be seen superimposed upon the basic waves of the left atrial pulse. With larger regurgitant flows (Fig. 1, *F* and *G*), the rise of the left atrial curve began early in systole and, in fact, partially encroached upon the isometric contraction phase of the left ventricle. The peak of the *v* wave approached the aortic diastolic pressure when the insufficiency was made massive enough, thus shortening or completely abolish-

ing the isometric relaxation phase of the left ventricle. This abbreviation of isometric relaxation tended to compensate to some degree for the huge leak, by enhancing the rapid phase of the left ventricular filling during early diastole.

Experiments designed to control the degree of regurgitation were carried out by inserting a graduated series of thin-walled tubes into the mitral orifice (Fig. 2). As mitral insufficiency became greater, a progressive increase in the end-diastolic pressure of the left ventricle was noted. At the same time, a marked

A.



B.

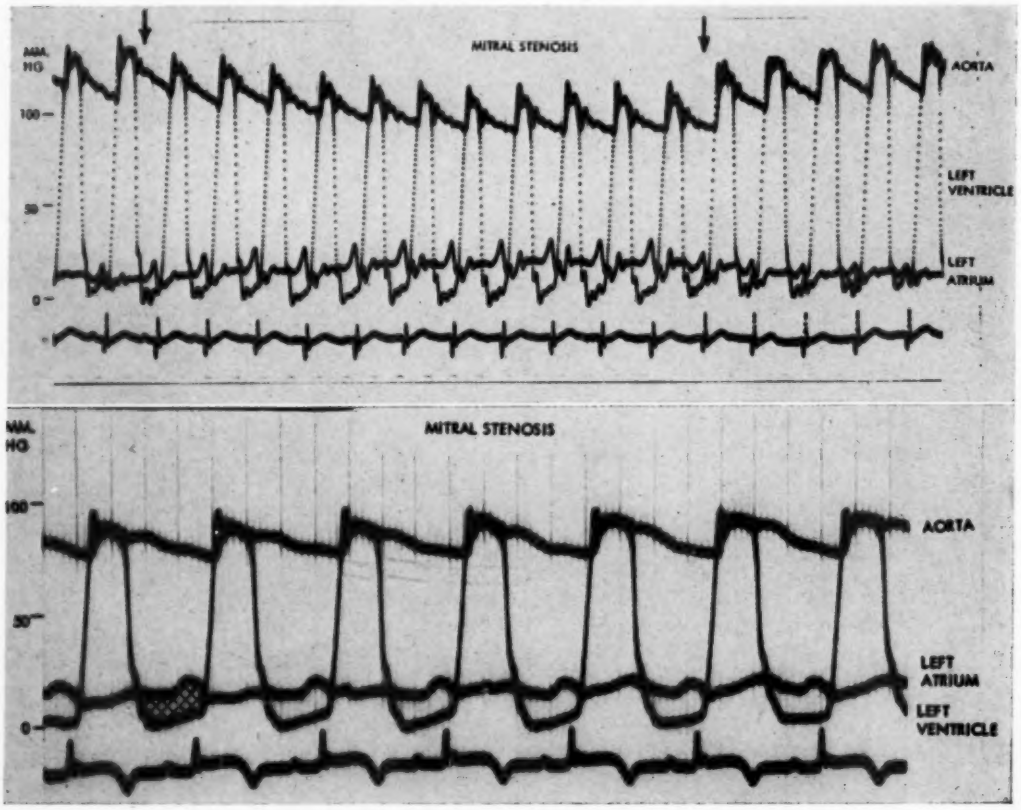
Fig. 4.—The effect of ligature compression above the aortic root in a normal dog (*A*) and a dog with mitral insufficiency (*B*). Aortic compression begins at the arrow to the left and is released at the arrow to the right. Note that the left atrial pressure rises only slightly in the presence of a competent mitral valve, while a comparable degree of aortic compression causes marked elevation of the left atrial pressure and prominence of the *v* wave when mitral insufficiency is present.

mitral reflux resulted in some lowering of the ventricular systolic pressure, as compared to control pressure in the same dog. The slope of the isometric contraction phase of the left ventricle did not change appreciably until the regurgitation was made so severe that marked cardiac dilatation and shock ensued (Fig. 2,*F*).

The normal *v* wave of the left atrial pulse usually does not exceed 8 mm. Hg. In this study, the height of the *v* wave in 17 dogs with varying degrees of acute mitral insufficiency ranged from 9 mm. to 55 mm., with an average height of 23 mm. The left ventricular end-diastolic pressure ranged from 3 mm. to 15 mm., averaging 9 mm.

The effect of ligature compression above the aortic root in a normal dog is contrasted with the response of a dog with mitral insufficiency in Fig. 4. With comparable degrees of aortic compression, the left atrial pressure of dogs with mitral insufficiency rose to a far greater extent than did that of normal dogs.

A.



B.

Fig. 5.—Mitral stenosis. In *A*, the suture encircling the mitral annulus is tightened at the arrow on the left and released at the arrow on the right. Note the magnification of the wave of atrial contraction and the appearance of an elevated pressure gradient in diastole between the left atrium and ventricle, following the production of mitral stenosis. In *B*, the left atrioventricular filling pressure gradient is crosshatched in the first beat.

2. *Mitral Stenosis.*—Simultaneous pressure recordings from the left atrium, left ventricle, and aorta in dogs with experimentally produced mitral stenosis are shown in Fig. 5. The location of the circumferential suture (anchored in the interatrial septum) used to produce mitral stenosis is shown in Fig. 6. The effect of tightening this suture in the plane of the mitral annulus is illustrated in Fig. 7.

The principal cardiodynamic change that occurs in mitral stenosis is elevation of the left atrial pressure level and the appearance of a diastolic pressure gradient between the left atrium and left ventricle. This differential pressure is caused by a combination of a rise in left atrial mean pressure during diastole and a coincidental fall in left ventricular diastolic pressure. The *a* wave of left atrial systole could be seen to grow progressively taller and broader as the stenosing suture was tightened, indicating the increased vigor of left atrial contraction and the pattern of response of the overfilled left atrium to augmented outflow resistance.

The elevated left atrial pressure in mitral stenosis resulted in delayed crossover of the left atrial and ventricular curves after the onset of ventricular systole, and premature crossover of left atrial and ventricular curves at the end of isometric relaxation during diastole. Both phenomena cause abbreviation of the isometric phases of contraction and relaxation of the left ventricle, thus providing slight increments of time for left ventricular filling.[15] The atrioventricular crossover points apparently signal the time of mitral valve closure and opening, and these valvular events take place at greater pressure levels and at moments when the ventricular pressure is rising or falling more rapidly than at the normal crossover points.

Fig. 6.—Mitral stenosis. The location of the stenosing suture encircling the mitral annulus is shown

The mean left atrioventricular filling pressure gradient in a series of 14 dogs with various degrees of mitral stenosis ranged from 9 mm. to 24 mm., and averaged 13 mm. Left ventricular end-diastolic pressure fell an average of 4 mm. following the tightening of the stenosing suture.

3. *Combined Mitral Stenosis and Insufficiency.*—The pressure tracings in representative dogs in whom mitral stenosis was acutely superimposed upon mitral insufficiency are shown in Fig. 8.

The immediate effect of constricting and releasing the circumferential suture about the mitral annulus can be seen in these illustrations. Acute mitral stenosis further reduced the compromised forward flow of mitral insufficiency, and the aortic pressure level fell in many instances. The elevated left atrioventricular

A.

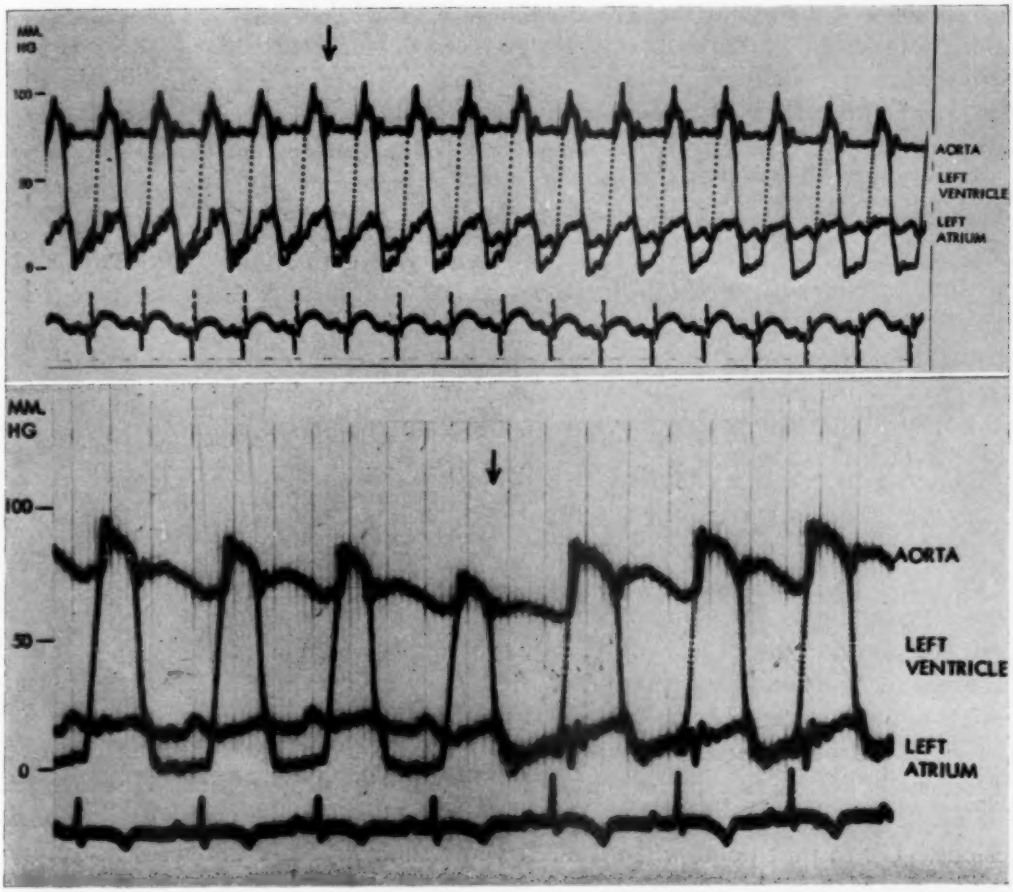
B.

Fig. 7.—Cross-sectional view of the mitral orifice. In *A*, the orifice is widely patent. In *B*, the orificial area has been markedly constricted by tightening the stenosing suture.

filling pressure gradient, characteristic of mitral stenosis, appeared as the circumferential suture was tightened. A striking feature of the combined lesion of mitral stenosis and insufficiency was the diminished prominence of the peak of the late systolic *v* wave, which ordinarily distinguished mitral insufficiency.

It can be seen from the curves in Fig. 8 that the left atrial pulse pressure narrows in this combined mitral lesion, and that the mean left atrial pressure rises. In other words, the superimposition of mitral stenosis on mitral insufficiency substitutes a high mean pressure for a wide pulse pressure in the left atrium.

A.



B.

Fig. 8.—Mitral stenosis and insufficiency. In *A*, the arrow denotes the onset of mitral stenosis in a dog with mitral insufficiency. Note the narrowing of the left atrial pulse pressure and the manner in which the prominent *v* wave is gradually obscured by the superimposition of stenosis. In *B*, mitral stenosis has been released at the arrow.

The width of the left atrial pulse pressure of 8 dogs with mitral insufficiency fell, on the average, from 17 mm. to 9 mm., when mitral stenosis was acutely superimposed, and the mean left atrial pressure rose an average of 7 mm. The end-diastolic pressure of the left ventricle in dogs with mitral insufficiency fell an average of 6 mm. when mitral stenosis was superimposed.

A summary of the average pressure values in 3 lesions, isolated mitral stenosis, isolated mitral insufficiency, and combined mitral stenosis and insufficiency,

is given in Table I. The absolute pressure values are obviously influenced by the altered hemodynamics of the open-chest preparation.

TABLE I. AVERAGE PRESSURE VALUES IN SINGLE AND COMBINED LESIONS OF THE MITRAL VALVE (MILLIMETERS OF MERCURY)

	MITRAL STENOSIS (14 DOGS)	MITRAL INSUFFICIENCY (17 DOGS)	MITRAL STENOSIS AND INSUFFICIENCY (8 DOGS)
Height (*a* wave)	24	10	16
Height (*c* wave)	15	16	13
Height (*v* wave)	16	23	18
Pulse pressure in left atrium	10	17	9
Left ventricular end-diastolic pressure	3	9	3
Left atrioventricular filling gradient (mean)	15	1	11

DISCUSSION

Wiggers and Feil[3] pointed out that with insufficiency of moderate degree there is little or no reflux through the mitral valve early in systole, since the speed of isometric contraction and the inertia of the blood in the left ventricle apparently delay the regurgitation until systole is well under way. The left atrial pulse in experimental mitral insufficiency may follow a variety of patterns depending upon the size of the insufficient orifice, the level of the aortic pressure, the turbulence of mitral flow, the volume elasticity of the left atrium and pulmonary venous bed, and the rapidity of left ventricular contraction. Small mitral leaks produce a barely recognizable accentuation of the late systolic *v* wave of the atrial pulse, which may be detectable only by comparison with a normal control tracing in the same animal. Huge regurgitant flows may elevate the left atrial pressure at the end of systole to a degree that equals or exceeds the aortic diastolic pressure. All gradations between these two extremes are possible in acutely produced lesions. Up to that point when the left ventricular myocardium loses its ability to contract vigorously, no change in the slope of isometric contraction takes place, despite a massive valvular regurgitation.

The onset of hypodynamic contraction of the ventricular muscle can convert a compensated degree of mitral insufficiency into a significantly greater one.[13] With myocardial depression secondary to anoxemia or rheumatic fever, the speed of isometric contraction may diminish permitting the low resistance mitral orifice to compete favorably or even preferentially with the aortic orifice, even during the early phases of systole. Moderate insufficiencies become massive ones under the influence of a combination of dilatation of the mitral ring and impaired contractility of the ventricular myocardium. For this reason, studies of the effect of experimentally produced mitral leaks or arrhythmias, such as atrial fibrillation, must be carried out with care, in order to avoid the superimposed effects of heart failure. Wiggers[14] long ago pointed out that atrial fibrillation was not responsible

for incompetency of the atrioventricular valves until heart failure and the dilated annulus ensued.

The effect of increasing outflow resistance of the left ventricle by partially occluding the aorta at its root was studied in normal dogs. It was found that only a minimal increase in left atrial pressure took place when the mitral valves were competent. It was pointed out previously that aortic compression resulted in a significantly greater rise in left atrial pressure when mitral insufficiency was present,[3,4,6] and this was confirmed by the present experiments. Conceivably, a direct clinical application may result from these observations. If vasopressor agents can be used safely to raise the systemic pressure of patients suspected of having mitral insufficiency, the characteristic and prominent elevation of the late systolic *v* wave of the left atrial pulse will become more easily detectable.

In mitral stenosis, numerous factors determine the height to which the left atrial pressure will rise. Chief among these factors are the cross-sectional area of the stenotic mitral valve, the change in mitral flow that takes place, and the elasticity of the pulmonary veins and left atrium. That the flow through the mitral orifice may fall during the acute production of mitral stenosis was demonstrated by the decided decrease in the aortic pressure that occurred when the stenosing suture was tightened. This was in accord with the findings of Katz and Siegel.[9] End-diastolic pressure of the left ventricle declined apparently in response to the decreased filling of the left ventricle that accompanied the stenosis. It is of interest that the left ventricular end-diastolic pressure occasionally was found to rise in patients following mitral valvulotomy.[15] A rising left atrial pressure in the presence of a static or declining left ventricular diastolic pressure is responsible for the appearance of the characteristic left atrioventricular filling pressure gradient of mitral stenosis. The reduction of this gradient is the physiologic objective of mitral commissurotomy.[16]

Considerable speculation exists concerning the exact mechanism of closure of the atrioventricular valves. Little[17] offered evidence that a transient reversal of the atrioventricular pressure gradient following atrial systole causes partial or complete closure of the atrioventricular valves before ventricular contraction begins. In mitral stenosis, there can be no such presystolic reversal in pressure gradient and the mitral leaflets must close abruptly from an open position. This provides an explanation for the accentuation of the first heart sound in mitral stenosis. The opening snap of the mitral valve may be due, similarly, to the wide separation of atrial and ventricular pressure curves immediately following their crossover point in diastole.[18,19] In addition, these crossover points in mitral stenosis occur at greater levels of pressure and at times when the ventricular pressure is rising or falling at a more rapid rate than at the normal crossover points. While the mitral leaflets in the normal heart may roll closed or float gently apart, the valve leaflets in mitral stenosis, subjected to these sudden and marked pressure gradients, can do little but shut abruptly in early systole and snap apart in diastole.

To a significant degree, the physiologic effects of combined valvular lesions are not merely a summation of those of the individual lesions. It appears that

the superimposition of mitral stenosis on mitral insufficiency markedly narrows the left atrial pulse pressure and obscures the characteristic peak of the late systolic regurgitant wave on the pressure curve. It can be argued that this is true because the stenosing suture has reduced the regurgitant volume, but from cardio-angiographic studies of this combined lesion,[20] it is clear that mitral reflux still takes place under these circumstances, although significant reduction in its size is not, of course, ruled out. This phenomenon of the camouflage of the pressure characteristics of mitral regurgitation when stenosis is superimposed makes clear the reason for the difficulty in the diagnosis of mitral insufficiency in patients with mitral stenosis from pulmonary capillary or direct left atrial pulses.

It is not completely valid to draw the inference that mitral stenosis compensates for mitral insufficiency to any significant degree. Although pressure peaks and regurgitant flows may be reduced by the superimposition of a stenotic lesion on an insufficient valve, the total level of pressure in the left atrium is not lowered. The resultant engorgement of the lungs is in no way alleviated. Only if pure annular dilatation of the mitral ring existed could it be expected that mitral stenosis would compensate for insufficiency without superimposing a new handicap on the circulation. Whether the left ventricle is protected from the deleterious effects of mitral insufficiency by superimposing mitral stenosis, it is difficult to determine with certainty from these acute experiments. Analysis of the pressure tracings shows a distinct decrease in the end-diastolic pressure of the left ventricle when mitral stenosis is produced on an already insufficient mitral valve. This would appear, at first, to alleviate appreciably the load on the left ventricle which faces the double task of supplying sufficient blood for forward flow into the aorta and the regurgitant volume into the left atrium. However, with the production of a tight mitral stenosis, mitral flow falls to a level sufficient to result in a significant fall in aortic pressure. Coronary artery flow, as a result, must diminish. In addition, the heart with mitral insufficiency can compensate for the regurgitation only if left ventricular filling is augmented during diastole. When immobile or restricted mitral cusps limit expansion of the valve orifice during diastole, one of the compensatory features of mitral insufficiency is removed. It can be seen that replacing a single mitral lesion with a double one is a two-edged sword.

SUMMARY

1. Simultaneous pressure pulses from the left atrium, left ventricle, and aorta were recorded from 39 dogs with acutely produced isolated mitral stenosis, isolated mitral insufficiency, and combined mitral stenosis and insufficiency.

2. Isolated mitral insufficiency was characterized by increased prominence of the *v* wave and widening of the pulse pressure of the left atrial curve. The slope of the isometric contraction phase of the left ventricle did not change appreciably until myocardial depression and shock ensued.

3. In mitral stenosis, magnification of the *a* wave of left atrial contraction occurred. An elevated atrioventricular pressure gradient appeared during the

filling phase of the left ventricle. The end-diastolic pressure of the left ventricle fell in response to the acute restriction of mitral flow.

4. The acute superimposition of mitral stenosis on pre-existing mitral insufficiency markedly narrowed the left atrial pulse pressure and obscured the prominence of the late systolic *v* wave seen in isolated mitral insufficiency.

5. The mechanism of opening and closure of the mitral valves was discussed and an explanation offered for the accentuated first sound and opening snap found in mitral stenosis.

6. Aortic compression in a dog with mitral insufficiency caused a far greater rise in left atrial pressure than in a normal dog.

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THE ELECTROCARDIOGRAM IN PATIENTS WITH POLYMYOSITIS AND DERMATOMYOSITIS

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POLYMYOSITIS is one of the so-called collagen diseases which was first described by Wagner[1] in 1863. It is a nonsuppurative, inflammatory, and degenerative disease of striated muscle without involvement of the skin. The late Dr. O'Leary, however, suggested that it is well to think of dermatomyositis as polymyositis with variable cutaneous lesions.[2] Excellent clinical and pathologic reviews have been published[3-6] on polymyositis and dermatomyositis. According to O'Leary, cardiac abnormalities are to be expected, especially in the severe cases of dermatomyositis with generalized muscular disease. He noted myocarditis with cardiac hypertrophy in some of these patients.

The present study was undertaken to determine whether the electrocardiogram would disclose abnormalities in patients with proved polymyositis and dermatomyositis.

During the period from January, 1950, through December, 1954, a total of 169 patients having polymyositis or dermatomyositis were encountered at the Mayo Clinic. Our paper will be limited to the electrocardiographic findings on 27 patients in whom the clinical diagnosis was confirmed by muscle biopsy or necropsy. Electromyograms were done on 26 of these patients; all results were reported as being compatible with those seen in diseases of skeletal muscles. An abnormal electromyographic finding alone is not pathognomonic of dermatomyositis or polymyositis, as it has been observed in other myopathies.[7]

Most of the patients whose electrocardiograms were reviewed for this study did not have symptoms or signs referable to the heart.

The literature on this subject indicates no unanimity of opinion with regard to the presence or absence of myocardial involvement. Günther[8] in 1940, stated that no electrocardiographic changes are found in polymyositis. Keil,[5] also in 1940, stated that the low voltage in dermatomyositis is due to increased resistance of the involved muscles, subcutaneous tissues, and skin to electrical current. Consequently, low-voltage complexes are not always a positive proof of myocardial disease.[5] In a case of dermatomyositis associated with hypertrichosis reported by Reich and Reinhart,[9] the electrocardiographic changes were interpreted as being due to variance of cutaneous resistance induced by aggravation of the

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disease (since the heart is not involved in dermatomyositis). In 1954, an author of a text on heart diseases stated that "the cardiac muscle has not been conclusively proven to be involved" in dermatomyositis.[10]

Several cases of myocardial involvement have been reported in the literature,[6,11-13] however, and in some of these cases the myocardial involvement was considered to be the cause of death. The most common electrocardiographic abnormalities according to Domzalski and Morgan[3] are low-voltage complexes, evidence of nonspecific myocardial injury, and both right ventricular hypertrophy and left ventricular hypertrophy with strain. Williams[14] interpreted the T-wave abnormalities of a 63-year-old patient with dermatomyositis as being due to generalized myocardial involvement such as is seen in anemia, malnutrition, and cachexia.

TABLE I. SUMMARY OF DATA

	MAYO CLINIC	LITERATURE
Total cases	27	26
Polymyositis	5	3
Dermatomyositis	22	23
Confirmation of clinical diagnosis		
Biopsy	25	17
Necropsy	2	9
Electromyogram (26 done)	26	—
Abnormality found	26	—
Sex		
Males	4	16
Females	23	10
Age, range in years	9–73	7–68
Mean, years	44.3	39.8*
Less than 40 years, patients	9	12
More than 40 years, patients	18	14
Temperature, elevated		
Range, °F.	99.8–102	100–103
More than 99.6° F., patients	4	9
Heart enlarged in x-rays	2	5
Heart murmur	9	3
Systolic	9	2
Diastolic	—	1
Necropsy		
Myocardial changes	1	2†
Normal heart	1	7

*Age of one adult not specified.
†Minor histologic changes were not considered significant.

CLINICAL DATA

Five of our 27 patients were given the diagnosis of polymyositis, and 22 had the combined muscular and cutaneous changes of dermatomyositis. There were 4 men and 23 women in the group. The mean age was 44.3 years.

Seven patients who were afebrile had pulse rates between 100 and 120 per minute, and only one of the 4 patients with temperatures of more than 99.6° F. had a ventricular rate of more than 100 per minute. Cardiac enlargement was evident in the roentgenograms of the thorax of 2 patients, without associated hypertension or evidence of valvular or coronary heart disease.

Physical examinations disclosed heart murmurs in 9 patients, all systolic in time and of low intensity with the exception of a "sea gull" murmur, Grade 4, in one patient. These murmurs were heard over all valve regions except that of the tricuspid valve.

Comparable data in 26 cases from the literature are listed along with our findings in Table I.

ELECTROCARDIOGRAPHIC AND HISTOPATHOLOGIC DATA

It was to be anticipated that the diffuse type of myocardial involvement presumably occurring in some cases of polymyositis or dermatomyositis would be reflected in a nonspecific type of electrocardiographic abnormality. On the basis of previous studies it seemed reasonable also to conclude that the electrocardiogram would probably be normal in the majority of patients with this disease.

In 19 (70 per cent) of this series of 27 patients the electrocardiograms were normal. A review of the literature indicates that 14 of 26 patients (54 per cent) had normal electrocardiograms[3,6,9,15-26] (Table II).

TABLE II. INTERPRETATIONS OF ELECTROCARDIOGRAMS IN PROVED CASES OF DERMATOMYOSITIS AND POLYMYOSITIS

	MAYO CLINIC	LITERATURE	TOTAL	
			NO.	PER CENT
Total cases	27	26	53	100
Normal electrocardiogram	19	14*	33	62
Low amplitude QRS in standard leads	5	5†	10	19
Myocardial involvement	2	2 ("myocarditis")	4	7.5
Conduction disturbance	0	4‡	4	7.5
Bundle branch block		2		
Intermittent sinoauricular block		1		
Auricular fibrillation		1		
Ventricular hypertrophy	1	1	2	4

*Necropsy in 4 cases, see text.
†Necropsy in 3 cases, see text.
‡Necropsy in 2 cases, see text.

The most frequent electrocardiographic abnormality in the remaining 8 patients in our series was a low-amplitude QRS complex in the standard leads

which was present in 5 patients (Fig. 1). The criteria used in the interpretation of low amplitude in the standard leads were deflections of less than 5 mm. in all QRS complexes.[27] The interpretation of the electrocardiograms from the literature was that of the author reporting each case. The observation that only 5 of

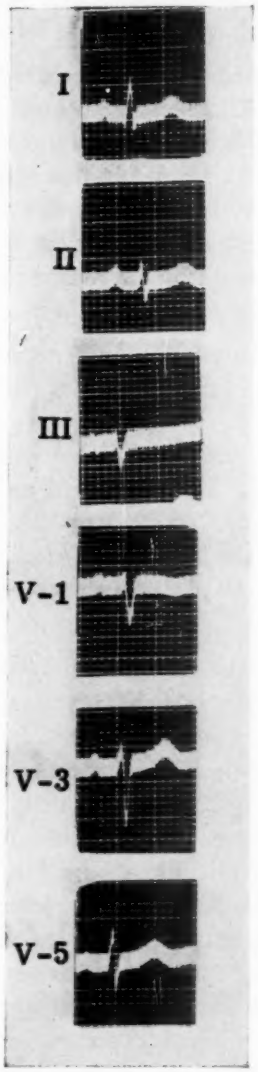

Fig. 1.—Typical electrocardiogram disclosing low amplitude of the QRS complexes noted in 5 of 27 patients.

the 27 clinic patients with extensive skin and muscle disease disclosed this abnormality seems to indicate that cutaneous resistance or other local factors in the extremities would not explain this abnormality and that it is perhaps related to myocardial disease. It seems to be somewhat similar to myxedema in this respect.

Electrocardiographic abnormalities indicative of previous anteroseptal myocardial injury, probably on the basis of coronary disease, were noted in two trac-

ings in each group. This does not suggest, however, that myocardial infarction is part of the disease process of polymyositis.

Disturbances of conduction and rhythm, such as intermittent[17-19] sino-auricular block and auricular fibrillation, have been reported, but we did not encounter any of these disturbances. One of the patients with the relic of myocardial infarction subsequently had incomplete left bundle branch block.

One patient had electrocardiographic evidence of left ventricular hypertrophy. The P-R interval was 0.12 to 0.18 second in 26 patients. In one patient it was 0.10 second. The QRS interval was 0.06 to 0.08 second in 23 patients, 0.10 second in 3 patients, and 0.12 second in one other patient. The Q-T interval was 0.32 second in one patient with a cardiac rate of 124 per minute. In another patient the Q-T interval was 0.40 second with a cardiac rate of 82 per minute. The amplitude of the T wave was 1.5 to 2 mm. in 17 patients, 2.5 to 3 mm. in 5 patients, 3.5 to 4 mm. in 2 patients, and 0.1 mm. in 3 patients.

Two of the 19 clinic patients who had normal electrocardiograms subsequently died of their disease, and necropsy was performed. The myocardium of one of these patients was normal. In this patient, mild changes of the rheumatic type were noted in the mitral valve, and the coronary sclerosis was Grade 1 (on the grading basis of 1 to 4). In the second patient many foci of small scars were present in the myocardium. These scars contained macrophages and lymphocytes. The histologic changes in the myocardium in this case were not similar to those in the skeletal muscle and were considered to be of a nonspecific type (Table II).

Necropsy was performed also in 9 of the cases reported in the literature. In 4 of these the electrocardiograms were normal. In one of these 4 cases a flabby heart was found; fragmentation and variation in size and shape of the fibers were evident.[15] The heart was normal in the second case except for interstitial edema and focal round-cell infiltration.[6] The hearts in the third and fourth cases were normal.[21-24] In 3 cases in which necropsy was performed the electrocardiograms showed low amplitude of the QRS complexes in the standard leads. In one of these 3 cases, necropsy disclosed an edematous myocardium with moderate atrophy, but without any changes similar to those in the skeletal muscle.[23] In the second case, pronounced interstitial edema of the myocardium was noted.[6] In the third case the mitral and aortic valves were sclerotic, the myocardium was pale but normal, and secondary fibrosis was present.[16] Necropsy in one case of conduction disturbance disclosed myocardial degeneration with round-cell infiltration and beginning connective tissue formation.[17] In another case with right bundle branch block the heart was found to be normal at necropsy except for a myxoma of the pulmonary valve.[18]

COMMENT

Hence, this study does not indicate clinicopathologic correlation as to the frequency, type, or nature of the myocardial involvement presumably occurring in polymyositis. The relative similarity of the electrocardiographic data in our

cases to those in the cases reported in the literature suggests that a nonspecific type of electrocardiographic abnormality is not unusual in patients with polymyositis, but occurs in only a minority of the patients.

SUMMARY AND CONCLUSIONS

The electrocardiograms of 27 patients given histologic and clinical diagnoses of dermatomyositis or polymyositis at the Mayo Clinic, from 1950 to 1954, and of 26 patients reported on in the literature were reviewed. Electrocardiograms were normal in 19 (70 per cent) of our patients. The electrocardiographic changes when present were relatively infrequent and were nonspecific in nature. Low amplitude of the QRS complexes of the standard leads was the most frequent abnormality. This was found in 5 of our 27 patients. Tachycardia, out of proportion to fever, was a rather common manifestation, since it was noted in 8 of our patients.

Arrhythmias and conduction disturbances were not noted in any of our patients, but a few were reported in the literature.

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THE SPATIAL VECTORCARDIOGRAM IN MITRAL VALVE DISEASE

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THE necessity for the proper selection of patients for mitral valvulotomy has led to intensive investigation and correlation of the clinical, hemodynamic, radiologic, and electrocardiographic features of mitral valve disease. However, relatively little information regarding vectorcardiographic findings in such patients has been available.[1-5] It is the purpose of this report to present the vectorcardiographic findings in 53 patients in whom the presence of mitral valve disease was confirmed at the time of surgery.

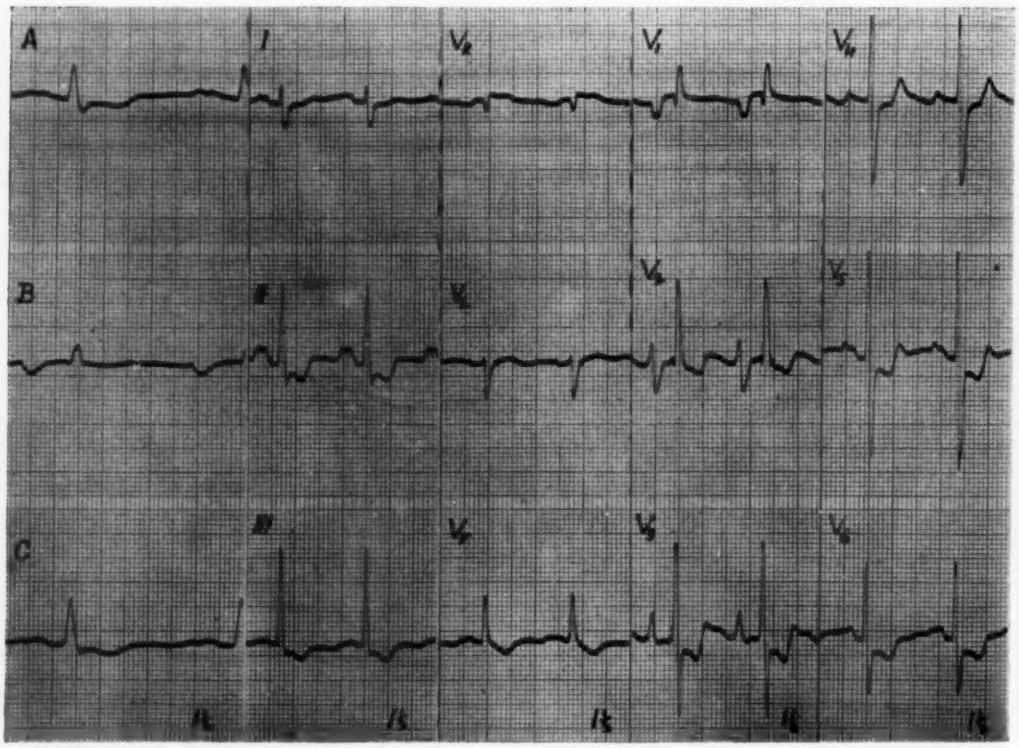

Fig. 1A.—Electrocardiogram of a 41-year-old woman in whom the presence of pure mitral stenosis and right ventricular hypertrophy was confirmed at post-mortem examination. Electrocardiogram taken at 50 mm./sec. and at 1.5 cm. = 1 mv standardization.

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MATERIAL AND METHODS

The 53 patients included in this report were studied at The Mount Sinai Hospital, New York. Their age range was from 26 to 50 years. Forty-one were women and 12 were men. In none of the patients studied was there any evidence, at the time of surgery, of rheumatic activity, organic involvement of other heart valves, hypertension, or coronary artery disease.

In 43 patients, "tight" mitral stenosis and the absence of a significant regurgitant jet were described at operation. In the remaining 10 patients, both mitral stenosis and a significant regurgitant jet were noted.

The vectorcardiograms were all recorded preoperatively using the cube system of electrode placement.[6] The vectorcardiograms were photographed from the screen of either a Technicon or Sanborn oscilloscope. Electrocardiograms were recorded with a Technicon three-channel, direct-writing cardiograph. Both the electrocardiographic and vectorcardiographic criteria recently described in this laboratory[7,8] for determining the presence of ventricular hypertrophy were employed in the analysis of the records.

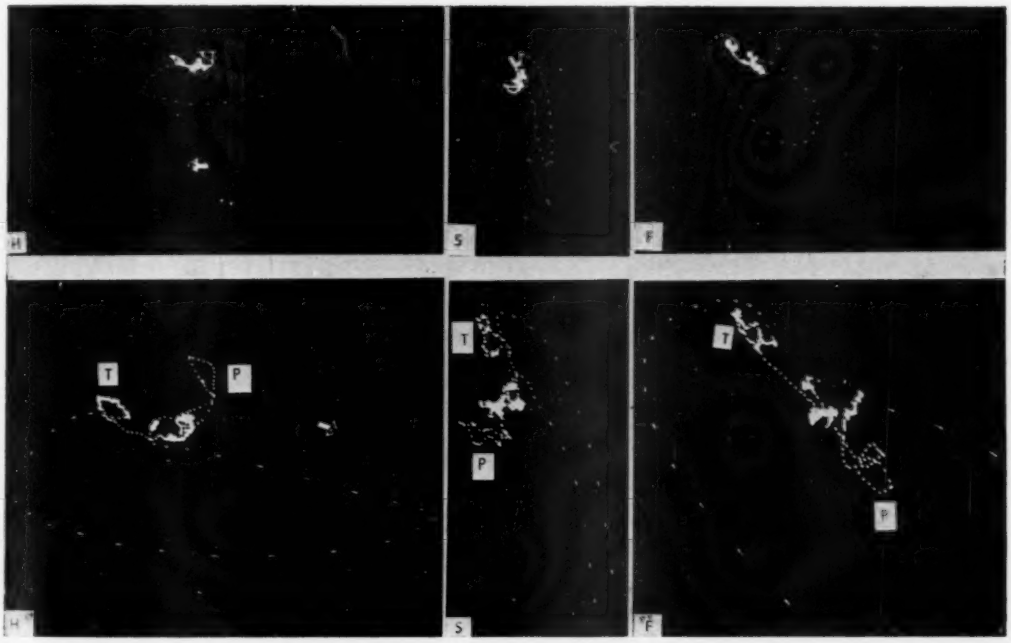

Fig. 1B.—Spatial vectorcardiogram of patient whose electrocardiogram is shown in Fig. 1A. *H* = horizontal plane, *S* = sagittal plane, *F* = frontal plane. This vectorcardiogram is typical of Group A (See text). Note the anterior orientation of the QRS loop, and its clockwise inscription. Note the large P loop, directed posteriorly, inferiorly and to the left in the magnified view below. Compare this with the normal P loop in Fig. 3.

RESULTS

I. *QRS Loop.—*

A. *Pure Mitral Stenosis.*—The vectorcardiograms in the 43 patients with pure mitral stenosis were divided into three groups on the basis of the vectorcardiographic configuration.

Group A: This group consisted of 16 patients in whom the vectorcardiogram revealed right ventricular hypertrophy as described in detail previously.[8]

The direction of inscription of the QRS loop in the horizontal plane was always clockwise, and the loop was oriented more to the right than the normal. The electrocardiograms revealed right ventricular hypertrophy in 14 of these patients and an rsR′ pattern in right precordial leads in the remaining two (Figs. 1*A* and 1*B*).

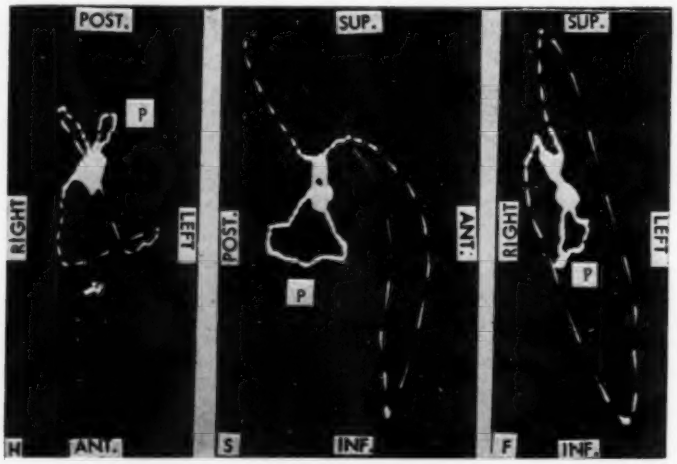

Fig. 2.—Spatial vectorcardiogram of a 39-year-old man with mitral stenosis, and a resting mean pulmonary artery pressure of 57 mm. Hg. The QRS loop is typical of Group B. It is oriented predominantly anterior to the isoelectric point, but is inscribed in a counterclockwise direction in the horizontal plane. Note the large P loop.

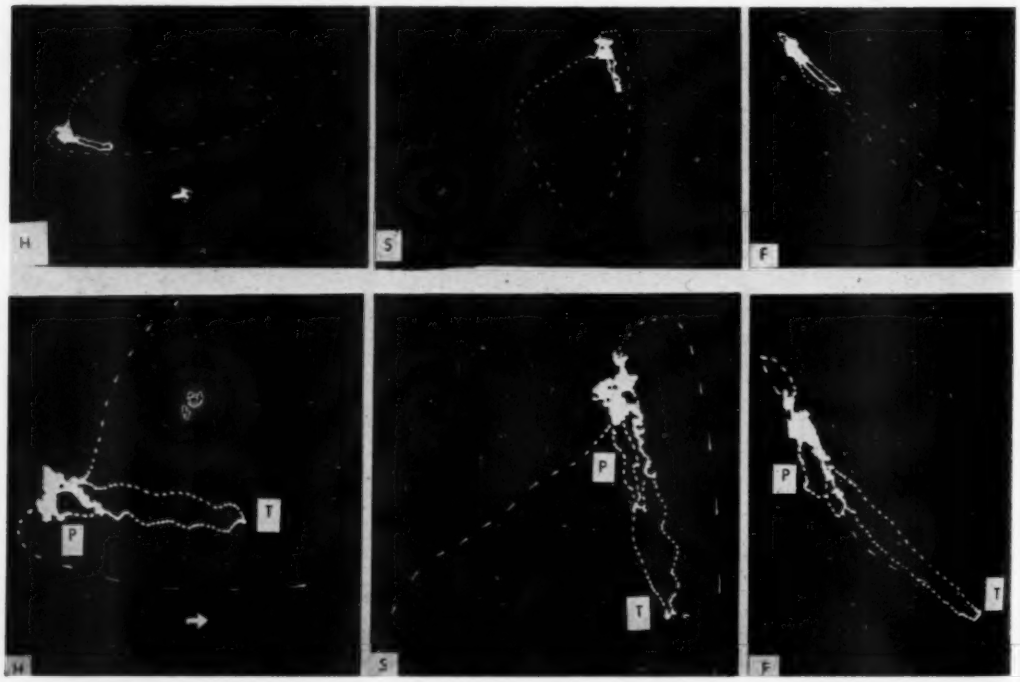

Fig. 3.—Spatial vectorcardiogram of a normal adult. In the magnified view shown below, the normal P loop is illustrated. Contrast this with the large P loops seen in Figs. 1B and 2.

Group B: This group consisted of 8 patients in whom the major portion of the QRS loop was located anterior to the isoelectric point, although the direction of inscription in the horizontal plane was counterclockwise (Fig. 2). This pattern may be found normally in infants and children[9] but was not observed by us in normal adults. It differed from the vectorcardiographic pattern of right ventricular hypertrophy as noted in Group A, in that the direction of inscription of the QRS loop in the horizontal plane was counterclockwise. In this group, the electrocardiograms showed right ventricular hypertrophy in 4 patients, no evidence of ventricular preponderance in 3, and an rsR′ pattern in right precordial leads in one patient.

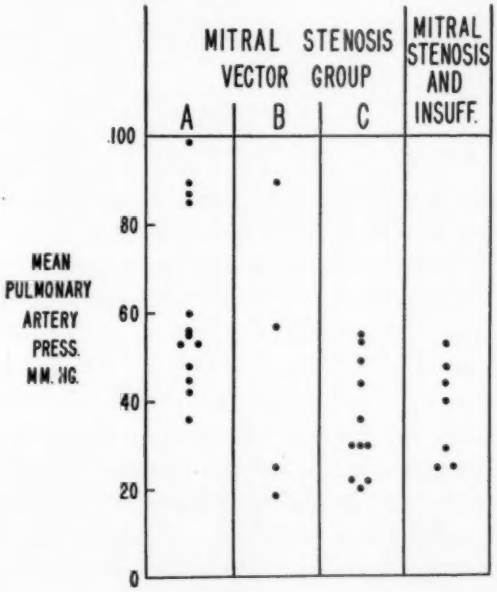

Fig. 4.—The relationship between mean pulmonary arterial pressure and vectorcardiographic configuration in patients with mitral valve disease.

Group C: The 19 patients in whom no vectorcardiographic evidence of ventricular hypertrophy could be detected were included in this group. The QRS loop was directed chiefly to the left, inferiorly, and somewhat posteriorly. The direction of inscription of the QRS loop in the sagittal and frontal planes was normal.[10] One of the electrocardiograms in this group showed the presence of right ventricular hypertrophy, while the remaining 18 showed no evidence of ventricular hypertrophy.

B. *Mitral Stenosis and Insufficiency.*—In the 10 patients with combined mitral stenosis and insufficiency, a normal balance of forces of the QRS loop was present in 9 patients, and left ventricular hypertrophy was present in one.[11] In none of the patients comprising this group was there electrocardiographic evidence of right ventricular hypertrophy. Post-mortem examination confirmed the presence of left ventricular hypertrophy in the single patient in whom the vectorcardiogram revealed this pattern.

II. *P Loop.*—

Normal sinus rhythm was present in 29 of the 53 patients studied. The P loops in these patients were, in general, larger than those encountered in normal subjects (Figs. 1*B*, 2 and 3). They were usually oriented posteriorly, inferiorly, and to the left of the isoelectric point. The P loops were often triangular in contour in the sagittal plane, with the apex of the triangle at the isoelectric point. No differences were apparent between the P loops of the patients with mitral stenosis and those of the patients with combined stenosis and insufficiency.

III. *Hemodynamic Correlations.*—

Although there was considerable overlap in the level of the resting pulmonary arterial pressures among the various groups, the pressures tended to be highest in patients whose vectorcardiograms showed right ventricular hypertrophy, Group A (Fig. 4).

DISCUSSION

Sixteen of the 43 patients with surgically proved mitral stenosis, without detectable mitral regurgitation at the time of surgery, demonstrated the vectorcardiographic findings of right ventricular hypertrophy previously described (Group A).[8] This pattern, however, may also be seen in the presence of associated left ventricular hypertrophy. It was noted in 2 pateints who had not undergone valvular surgery because of clinical evidence of regurgitation, and who, therefore, were not included in this series. At necropsy, in both patients, mitral insufficiency and left ventricular hypertrophy were present, in addition to the mitral stenosis and right ventricular hypertrophy. The left ventricular hypertrophy was not apparent vectorcardiographically, because the mitral stenosis produced marked right ventricular hypertrophy which electrically overbalanced the hypertrophied left ventricle. In addition, 8 patients presented a vectorcardiographic configuration in which the QRS loop was located primarily anterior to the isoelectric point, but was inscribed in a counterclockwise direction in the horizontal plane (Group B). This pattern has been noted in mitral stenosis by Deglaude and Laurens.[3] We observed this type of vectorcardiogram in 2 patients following a successful pulmonary valvulotomy for pulmonic stenosis. In both patients, the preoperative vectorcardiogram exhibited the usual pattern of right ventricular hypertrophy (with clockwise inscription in the horizontal plane). We believe that the vectorcardiographic configuration seen in patients in Group B represented right ventricular hypertrophy on the basis of the following observations:

1. This pattern has been seen in very young normal infants (who had physiologic right ventricular hypertrophy).[9]

2. In adults, this configuration has been observed in association with lesions imposing a hemodynamic burden on the right ventricle, such as primary pulmonary hypertension (post-mortem confirmation)[12] and postoperative pulmonary stenosis, as previously noted.

3. This type of vectorcardiogram has not been observed in normal adults in this laboratory.

A striking difference was observed between the frequency with which the vectorcardiogram detected the presence of right ventricular hypertrophy in patients with mitral stenosis and those with congenital malformations imposing a hemodynamic burden on only the right ventricle.[8] Twenty-four of 43 patients with mitral stenosis (56 per cent), and 62 of 66 patients with congenital heart disease (94 per cent) had vectorcardiographic evidence of right ventricular hypertrophy. The reasons for this discrepancy may be related to the following factors:

1. The hemodynamic burden in the congenital cardiac group appeared earlier in life, and frequently was of longer duration than in the patients with mitral stenosis.

2. The hemodynamic burden, as expressed by the right ventricular work, was frequently greater in the patients with congenital heart disease than in the patients with mitral stenosis.

3. None of the patients with right ventricular hypertrophy and congenital heart disease had any lesion imposing a burden on the left ventricle.[7] In none of the patients with mitral stenosis was there evidence of either rheumatic activity or associated valvular lesions, as determined by both clinical examination and surgical exploration. However, mild valvular abnormalities or low-grade rheumatic activity, both of which may escape detection, may influence the size of the left ventricle. These factors, therefore, may influence the vectorcardiographic configuration.

SUMMARY AND CONCLUSIONS

1. Spatial vectorcardiograms were recorded in 3 planes in 53 patients with mitral valvular disease (the diagnosis was confirmed at surgical exploration).

2. The vectorcardiogram detected right ventricular hypertrophy in 24 of the 43 patients with pure mitral stenosis, while the electrocardiogram, employing recently published criteria, detected right ventricular hypertrophy in 19.

3. The vectorcardiogram showed a normal balance of electrical forces in 19 of 43 patients with pure mitral stenosis, and in 9 of 10 patients with mitral stenosis and significant regurgitation.

4. A normal balance of vector forces was not encountered in patients with a resting mean pulmonary artery pressure above 55 mm. Hg. The right ventricular hypertrophy configuration seen in patients in Group A was not observed in patients with a resting mean pulmonary artery pressure below 35 mm. Hg.

5. Enlarged P loops, directed posteriorly, inferiorly, and to the left, were frequently noted among the 29 patients with sinus rhythm.

The cooperation of Dr. M. M. Ravitch, who performed most of the valvulotomies, and of Dr. A. J. Gordon, under whose direction the cardiac catheterizations were performed, is gratefully acknowledged. We also wish to thank Miss Ruth Jaspan for her technical assistance.

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FURTHER STUDIES ON RHEUMATIC FEVER EPIDEMIOLOGY

Comparative Incidence of Rheumatic Fever, Streptococcal Carriers, and Antistreptolysin Titers in the Tropics and in Mexico City

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RHEUMATIC fever occurs most commonly in the temperate zones. It is rare in the tropics[1,2] and in the arctic regions. A survey by Nichol[3] disclosed that the hospital admission rate for patients with rheumatic disease was 10 times higher in Boston than in Miami, and Coburn[2] reported that the subsidence of the rheumatic activity after the transference of 10 rheumatic children from New York to Puerto Rico suggested that the beneficial effect was due to the lower incidence of upper respiratory infections in the tropics.

In a previous communication[4] we stressed the lower figures for cases of rheumatic fever from our tropical zones as compared with the figure on patients coming to the National Institute of Cardiology from regions having a temperate climate. Our sample included 13,426 cases from Mexico City, and 145 from the states of Chiapas, Nayarit, and Tabasco, where the tropical rainy climate predominates. The ratio of rheumatic cases to the total cases of heart disease (r/t index) was 0.5990 for the inhabitants of Mexico City, and only 0.0967, or lower, for the individuals coming from places enjoying a tropical climate.†

In order to explain such different r/t indices on a geographic basis, we decided to perform the present "pilot" study (devoted to examining the incidence of rheumatic fever, pharyngeal flora (for *Streptococcus hemolyticus*), and antistreptolysin "O" titers) on a group of students living in Tapachula (in the state of Chiapas) which has a tropical rainy climate, and to compare our findings with similar data obtained from a sample group in Mexico City, which has a temperate rainy climate.

MATERIAL AND METHODS

For studying the incidence of rheumatic fever in Tapachula, one of us examined a group of 300 high school and college students of the locality. Their mean age was 16.47 years. Seventy-eight per cent were men, and twenty-two

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†The figures are significative by simple inspection and X^2 gives a "p" many times larger than 0.001 (not in the table).

per cent women. This group was compared with a group examined by Robles Gil[5] in Mexico City, which included 340 individuals from 15 to 30 years of age.

In March 1956, within a two-day difference, throat cultures were made from 102 students from Tapachula and from 100 from Mexico City (mean age of this latter group 14.52 years). The procedure was as follows: Sterile swabs were gently rubbed over both the tonsillar areas and the pharyngeal wall, and blood-agar plates were at once inoculated and placed in the incubator at 37° C. Readings were made after 24 and 48 hours, by simple inspection, and the colonies showing beta hemolysis were isolated for further microscopical examination and (Lancefield's) group classification. Antistreptolysin "O" titers were investigated in the sera of 58 students from Tapachula and also in 42 samples from normal individuals living in Mexico City. Todd's method was followed and the unit content of each specimen per milliliter[3] was expressed as the reciprocal of the serum's highest dilution able to inhibit hemolysis.

RESULTS

1. *Incidence of Rheumatic Fever in Tapachula and in Mexico City.*—No manifestations of active or inactive rheumatic fever were found in the group from Tapachula. This nonexistence of the disease if compared with the figure of 0.88 per cent given by Robles Gil for the group examined in Mexico City is of interest, even though it is not statistically significant at the 5 per cent level (number expected in 300, 2.64, and S.D. 1.61).

2. *Incidence of Hemolytic Streptococcus in the Throat of the Two Groups.*—Streptococcus producing beta hemolysis were isolated in 14 of the 102 specimens obtained in Tapachula; of these, 3 strains belonged to Lancefield's group "A" and 11 to group "G." From the 100 cultures made in Mexico City, one strain belonging to the animal group "C," and another one corresponding to the human group "A" were obtained.

3. *Antistreptolysin "O" Titers.*—This antibody was found to give higher titers in the sera from the students of Tapachula, the mode being for this sample 200 U. and for the sample of Mexico City, 100 U. If as Paul and associates[6] admit, cases having a titer of 200 or higher are to be considered as above normal, the incidence of abnormal titers was 55.13 per cent for Tapachula and only 35.70 per cent for Mexico City (X^2:3.70, which very nearly approaches a significant value at the 5 per cent level). Detailed results are shown in Table I.

TABLE I. ANTISTREPTOLYSIN "O" TITERS IN SERA FROM NORMAL INDIVIDUALS FROM TAPACHULA AND MEXICO CITY

TITERS (UNITS)	MEXICO CITY (42 CASES)	TAPACHULA (58 CASES)
Less than 100	15 (35.71%)	11 (18.96%)
100	12 (28.57%)	15 (25.86%)
200	9 (21.42%)	24 (41.37%)
300	5 (11.90%)	4 (6.89%)
400	1 (2.38%)	4 (6.89%)

DISCUSSION

Our data confirm the lesser incidence of rheumatic fever in the tropics. The lack of rheumatic cases in the sample from Tapachula, even if it lacks statistical significance, becomes of value if one takes into consideration the analogous findings reported by other authors and, in our case, of the extremely significant difference in the r/t indices we found between zones having a temperate and a tropical climate.

Our studies also show that Lancefield's "A" streptococcus is as prevalent in the throats of the people from the tropics as in the throats of those from Mexico City, so that the rarity or absence of rheumatic fever in the tropics cannot be attributed to a lesser contact of the population with streptococci or its products.

In fact, if one takes into account the higher antistreptolysin values found by Paul and associates[6] in Havana (Cuba), the larger amount of streptococcal antitoxin in the tropical sera examined by Plummer,[7] and our own findings in relation to the differences in streptolysin titers in the two samples we examined, the conclusion is obvious that "subclinical infections must be prevalent and take place earlier in the tropics than in the temperate climate."[7]

It could be argued that the high incidence of streptolysin "O" producing group "G" streptococcus in the throat samples from Tapachula (nearly 11 per cent) could be considered as the reason for the higher antistreptolysin "O" titers already referred to, but infections from group "G" streptococcus in the human being seem to be rather exceptional,[8,9] even with bacteria belonging to this group inhabiting the nose, throat, vagina, and feces of normal individuals[10] (i.e., without producing infectious symptoms). Therefore, we consider our finding of animal pathogenic groups "C" and "G" hemolytic streptococcus in the throat of some of the students we examined as devoid of clinical and immunological significance.

The problem remains of reconciling our epidemiological data which show a higher prevalence of streptococcal infections but a very much lower incidence of rheumatic fever in the tropics. Since Coburn's studies seem to indicate that it is the climatic change which influences the rheumatic process to become either dormant or activated, there seems to be no alternative explanation other than to indicate the salutary effect of the tropical climate as being due to a changed reaction on the part of the host in the face of rheumatogenic infection. Urine of rheumatic children may have a lower content of 17-OHCS,[11] but the figures so far obtained cannot be taken as truly indicative of the hormonal response to the rheumatic agent. It is to be expected that further studies will show the possible different behavior of the hypophysocortical axis in relation to streptococcal infection and to climate.

CONCLUSIONS

1. Rheumatic fever has a much lower incidence in tropical zones than in those having a temperate climate.

2. No rheumatic fever was discovered in 300 high school and college students from Tapachula (state of Chiapas) a region having a tropical climate. This figure is

not, however, statistically significant if compared with that reported by Robles Gil for Mexico City (3 rheumatic individuals in a sample of 340).

3. Throat blood-agar cultures were positive for Lancefield's "A" streptococci in 3 out of 102 specimens taken in Tapachula. The incidence of positives was one per cent at the same time in Mexico City.

4. Antistreptolysin titers were higher for the serum samples taken in Tapachula (200 U.) than for those obtained in Mexico City (100 U.).

5. Since streptococcal infections seem to be as prevalent (or even more prevalent) in the inhabitants of the tropics as in populations from temperate zones, and since rheumatic fever is rare in tropical regions, it is suggested that climate acts by changing the response of the host before the rheumatogenic infection.

SUMMARY

It is generally agreed that rheumatic fever is more prevalent in temperate than in tropical zones. It has also been stated that the salutary effect of the tropics on rheumatic patients may be due to the lower incidence of upper respiratory infections in regions enjoying a tropical climate.

The present study confirms the rarity of rheumatic disease in the tropical zones of Mexico, but also shows that the rate of streptococcus carriers is as high in the tropics as in temperate regions. It also gives data showing that antistreptolysin titers are higher in the sera from persons inhabiting the tropics, thus pointing to the greater prevalence of streptococcal infections in tropical zones.

The above considerations suggest that the tropical climate affects the response of the host before the rheumatogenic agent.

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FURTHER REMARKS ON THE SYNDROME OF ABERRANT A-V CONDUCTION (WOLFF-PARKINSON-WHITE)

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THE subject of aberrant atrioventricular conduction has not completely emerged yet from its theoretical realm. This is because the available histologic observations are few in number and the experimental evidence is not yet conclusive. It seems, at least from the report that follows, that there is still room for clinical observations, theoretical considerations, and perhaps for even some quite plausible conclusions based on these considerations.

In previous communications[1-4] various observations were recorded regarding the subject of the mechanism of the syndrome in question, the arrhythmias with which the Wolff-Parkinson-White (WPW) syndrome is frequently associated, and the effects of drugs, particularly of the cholinergic group, on the components of this electrocardiographic complex. In this paper, the author intends to discuss briefly one or two points already referred to in previous reports, and to illustrate a number of observations heretofore not reported, with the hope of further elucidation of the peculiarities of this interesting syndrome.

Effect of Digitalis.—The effect of digitalis on the WPW syndrome was noted in a previous paper.[1] For some reason, this effect cannot be obtained in every case of WPW syndrome. Fig. 1,*A* shows the three standard leads of an electrocardiogram secured prior to the intravenous administration of 0.34 mg. of strophanthin. Thirty minutes later the electrocardiogram presented the typical configuration of the WPW (Fig. 1,*B*). It is assumed that only a case with a vulnerable A-V node will show this response. By blocking the A-V conduction with digitalis, the sinus stimulus is diverted into the accessory pathway. The resistance of the A-V node to cholinergic influence (digitalis) is a feature varying with the individual. It is to be recalled that, generally, the effect of digitalis on the electrocardiogram is not constant for all individuals, each case however, reacting to the drug repeatedly in the same manner (RST deviations).

Fig. 2,*F* illustrates another effect of digitalis on the WPW syndrome, namely, the apparent widening of the QRS complex. This tracing was recorded after a full digitalizing dose of the leaf was administered in the course of 24 hours. The widening of the QRS in this case seems to be due to the fusion of the P wave with the delta component of the QRS complex. The delta component of the abnormal QRS complex is apparently a labile electrocardiographic structure, and may, under certain circumstances, be dislocated from its usual position at the onset of the QRS complex.

Positional Changes.—Fig. 2 illustrates some of the changes which may occur in the WPW syndrome with change of position. Fig. 2,*A* is a tracing secured with the patient in a prone position. Fig. 2,*B* was obtained in the same position, with the chest fixed in a deep inspiratory phase. Note the isolation of the delta wave and the thinning of the upstroke in Leads II and III. Fig. 2,*C* was obtained after a full expiration. Note the structure of the delta wave and the resultant width of the QRS complex. Fig. 2,*D* was taken when the patient was lying on the right side, and

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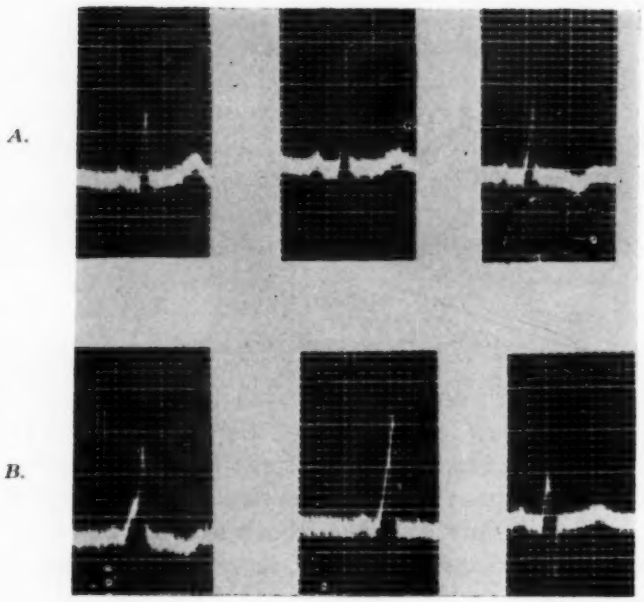


Fig. 1.—The effect of strophanthin on the WPW syndrome. *A*, Tracing secured immediately prior to the administration of 0.34 mg. of strophanthin intravenously. *B*, Tracing secured 30 minutes after the intravenous administration of strophanthin.

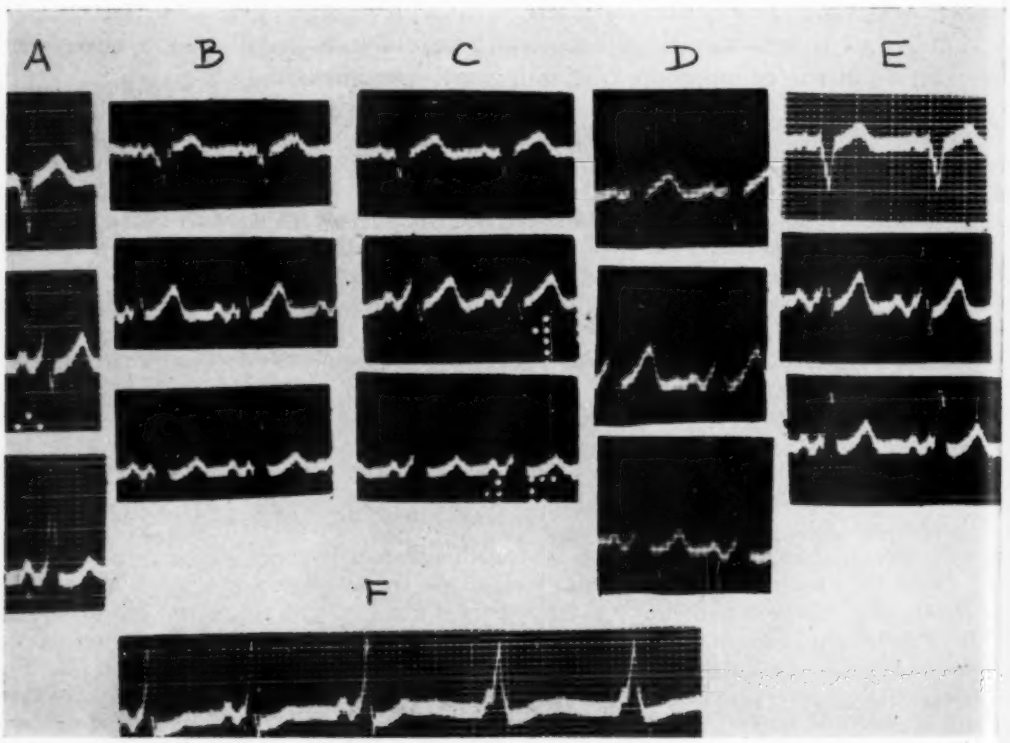


Fig. 2.—*A*, Tracing obtained with the patient in the prone position (standard leads). *B*, Tracing obtained in the prone position on deep inspiration. *C*, Tracing secured in the prone position on deep expiration. *D*, Tracing secured with the patient on his right side. *E*, Tracing secured with the patient on his left side. *F*, Effect of digitalis on the same patient. Note effect on the QRS width (Lead II).

Fig. 2,*E* when on the left side. This case illustrates the lability of the delta wave as far as its location is concerned, and the dependence of the QRS width and shape on the location of this special electrocardiographic component.

Another effect of position on the WPW syndrome in an 80-year-old woman is depicted in Fig. 3. Fig. 3,*A* was secured with the patient in a prone position (Lead I). Fig. 3,*B* is the same lead obtained in the right lateral position, and Fig. 3,*C* in the left lateral position. Figs. 3,*B* and *C* present normal sinus cycles. Changing back the patient's position to the prone or sitting position

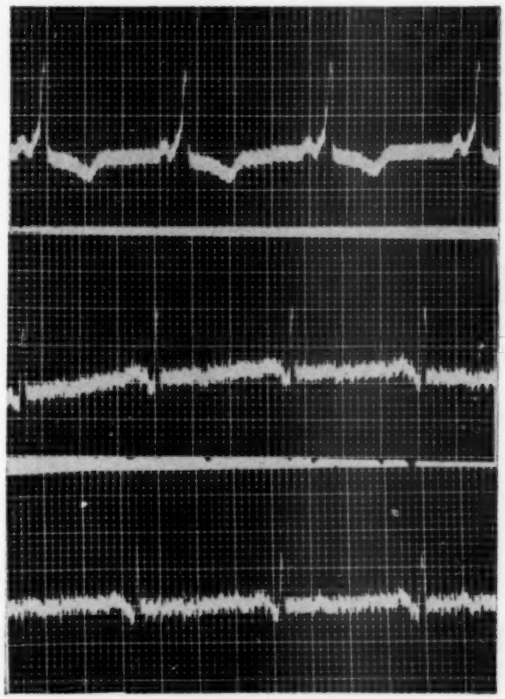


Fig. 3.—*A*, Lead I in the prone position. *B*, Lead I in the right lateral position. *C*, Lead I on the left lateral position. Unusual effect of change in position. Vagus effect?

reversed the tracing again to the WPW syndrome configuration. Fig. 4 further illustrates some of the positional changes that can occur in the WPW syndrome. Fig. 4,*A* was secured in the sitting position, Fig. 4,*B* in the supine position. In Fig. 4,*A* the P wave is apparently isoelectric. In Fig. 4,*B* the delta wave migrated downward somewhat. Fig. 4,*C* was obtained on the following day in the supine position. Fig. 4,*D* was secured in the right lateral position. Note again the change in the shape and location of the delta wave. Incidentally, the amplitude of the QRS is diminished without affecting the degree of the R-T segment negativity. In Fig. 5 (80-year-old woman), *A* was obtained in the prone position, *B* in the sitting, and *C* in the standing position. Only the standard leads were recorded. Note the change in the structure of the P wave, isolation of the delta wave, the dependence of the QRS width on the position of the delta wave, changes in amplitude of the QRS complex, the sinus arrhythmia (a vagus tone function), and, what is very important, the direction of RS-T-I and RS-T-III. One can easily mistake this tracing for one indicative of an acute posterior myocardial infarct.

The RS-T Segment.—The RS-T segment in the WPW syndrome is an intriguing phenomenon. Fig. 6 presents two WPW syndrome tracings of a 32-year-old man with a minimal case of pulmonary tuberculosis. Fig. 6,*A* was obtained on Oct. 27, 1955; Fig. 6,*B* on Dec. 7, 1955. Three normal tracings were secured in the interval between these dates, and a normal tracing was also recorded

a few hours after tracing 6,*B* was taken. A normal ballistocardiogram was also recorded on the same day. Clinically, nothing abnormal was observed in the patient's behavior between Oct. 27, 1955, and Dec. 7, 1955. The obvious change in the R-T segment occurred without an obvious cause. A remote possibility perhaps, as an explanation for the change, is the positional uncertainty

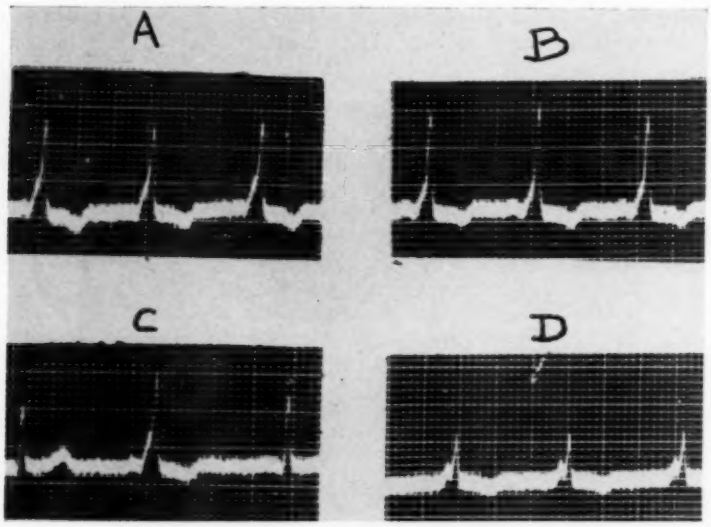
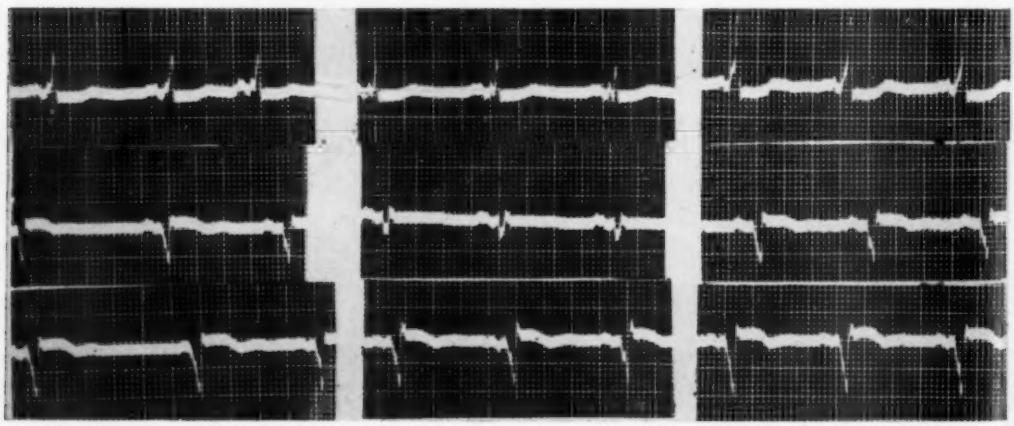


Fig. 4.—*A*, Tracing secured in the sitting position. *B*, Tracing of the same patient secured in the supine position. *C*, Tracing secured on the following day in the supine position. Note WPW syndrome beat situated between two normal beats. *D*, Tracing secured in the right lateral position on the day *C* was obtained.



A. *B.* *C.*

Fig. 5.—*A*, Standard leads obtained in the prone position. *B*, Standard leads of the same patient in the sitting position. *C*, Standard leads secured in the standing position. (See text.)

of the mediastinum in cases of pulmonary tuberculosis. This speculative idea emerges from the positional change of the delta wave in aV_L, and the appearance of the QRS complex in V_5 and V_6. That the positional change of the mediastinum can influence the R-T segment in the WPW syndrome can be attested by Fig. 7. All sections in this figure represent Lead I. *A* was takea in

the supine position, *B* in the supine position on expiration, *C* in the supine position on inspiration, *D* in the right lateral position, and *E* in the left lateral position. Note the positivity of the T wave in *C* and *E*, in association with a diminished amplitude of the QRS complex. On deep inspiration, and in the left lateral position, the heart rotates clockwise, and the tendency to right-axis deviation takes place, with consequent lowering of QRS-I, and deepening of the T wave in aV_R. The lowering of the P wave in these situations or its disappearance is an associated phenomenon.

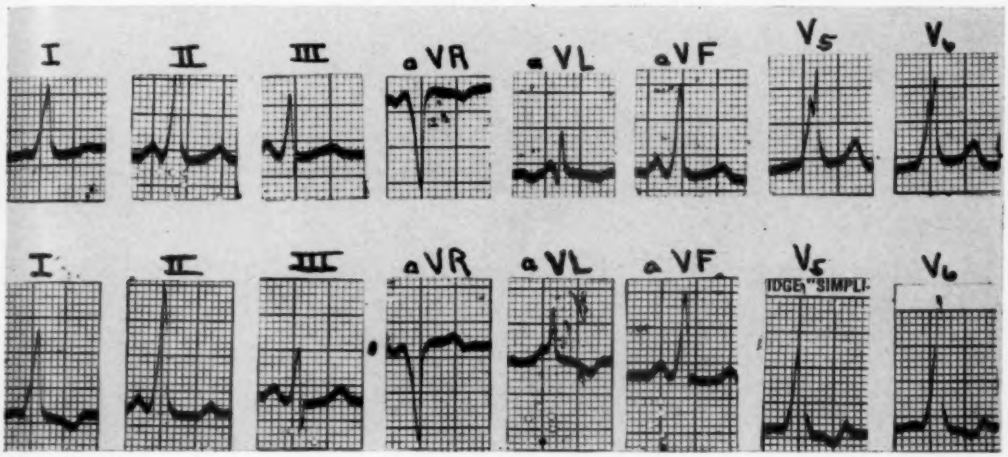


Fig. 6.—*A*, Tracing obtained on Oct. 27, 1955. *B*, Tracing of the same patient on Dec. 7, 1955. Note spontaneous RS-T changes.

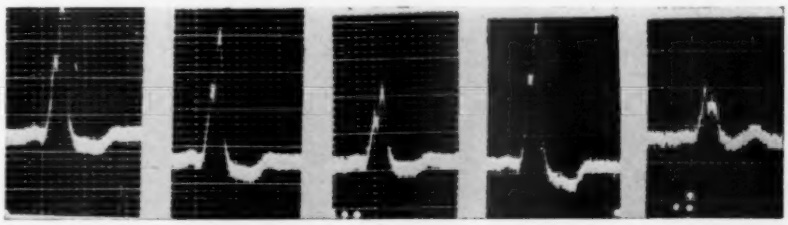


Fig. 7.—*A*, Tracing secured in supine position. *B*, Tracing secured in supine position on expiration. *C*, Tracing secured in supine position on inspiration. *D*, Tracing secured in right lateral position. *E*, Tracing secured in left lateral position. (Note changes in the configuration of the RS-T segment.)

On the other hand, the changes in the R-T segment in the WPW syndrome tracing may in some cases have an organic significance. Fig. 8 presents 3 tracings of a man 26 years old, first seen in January, 1945. Fig. 8,*A* is the tracing secured on that date. A rough systolic murmur was audible over the base of the heart and a soft systolic murmur at the apex. Although no history of rheumatic fever was obtained, it was thought that the murmurs represented a rheumatic valvulitis. Several similar tracings were secured in the course of the next few years. In September, 1955, the patient presented signs of cardiac failure, a double murmur at the base, and a one-finger spleen. Subacute bacterial endocarditis was suspected. Fig. 8,*B* was secured on that occasion. Note the change in the amplitude of the P wave, suggestive of auricular enlargement. The RS-T segment changes are particularly conspicuous, and like the P wave, are probably an expression of myocardial damage. Two months later the patient died in congestive failure. The necropsy

revealed healed subacute bacterial endocarditis, with involvement of the aorta, mitral and tricuspid valves. Ten days prior to the patient's death an electrocardiographic tracing was secured which, for the first and only time, revealed a non-WPW syndrome configuration. A first stage A-V block was noted in addition to some S-T-II depression.

A-V Block.—The subject of A-V block in cases with the WPW syndrome is particularly fascinating because it is basic. The presence of A-V block should divert the sinus impulse to the aberrant pathway. If this does not occur, it is a reasonable assumption that the aberrant channel has a higher degree of block. In a disseminated myocardial lesion such as is conceivable in an active rheumatic process, the aberrant pathway may be blocked so much that the impulse will travel through the partially occluded A-V path.

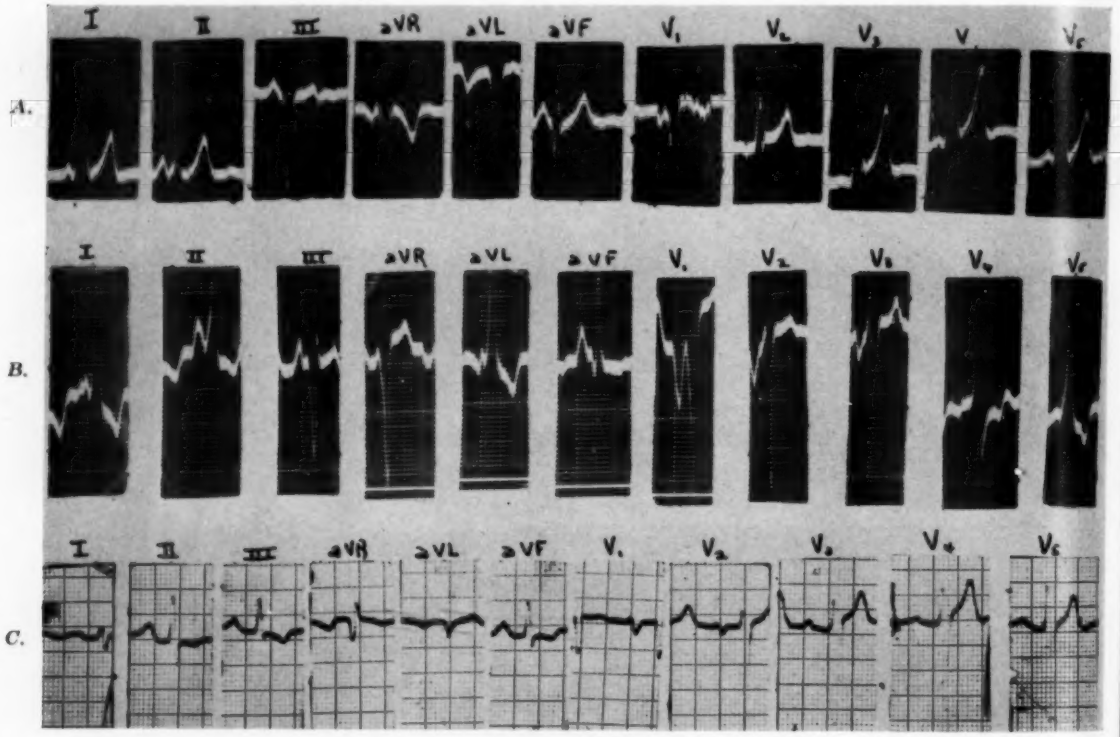


Fig. 8.—RS-T changes of possible "organic" significance. *A*, Tracing secured in January, 1945. *B*, Tracing secured in September, 1955. *C*, A normal conduction tracing secured in November, 1955.

That the aberrant pathway is subject to block can be seen in Fig. 9. Fig. 9,*A* is the control Lead I of a 74-year-old patient with coronary sclerosis. Note the normal structure of the P wave. Fig. 9,*B* is Lead I of the same patient, showing WPW syndrome. Note the similarity of the blocked P wave with the one preceding the abnormal QRS complex. This probably means that the block is in the accessory pathway. If a block can exist in the aberrant channel, then the P-R interval of the WPW syndrome does not always necessarily have to be short. Such is the case in Fig. 10, where the WPW syndrome is associated with a normal P-R interval. It thus appears that the only important criterion for the WPW syndrome is the presence of a delta wave (P-R interval may by normal and the QRS complex does not have to be wide). It is this delta wave that helps to distinguish the WPW syndrome beat from the fusion beat in the occasional case where such differentiation is essential.

Fusion Beats.—Fig. 11 (Lead II) presents a series of variations of fusion beats observed in a 49-year-old patient with pulmonary tuberculosis, right pneumothorax, and arteriosclerotic heart

disease with congestive failure. It is to be noted that the width of the QRS complex depends on how much of the P-R interval, or actually the P wave itself, is engulfed by the QRS complex. When the P wave is no longer discernible, the QRS complex seems the widest. It then assumes the contour of a ventricular ectopic beat, no longer influenced by the stimulus transmitted from the

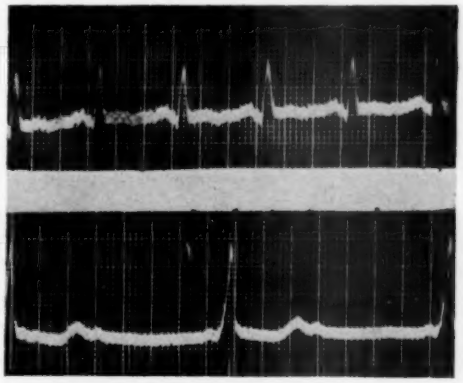


Fig. 9.—*A*, Normal sinus beats normally conducted through the A-V node. Lead I. *B*, WPW-beats with 2:1 block in same patient. The structure of the P wave in the blocked beats is the same as in the nonblocked, but different from those in *A*.

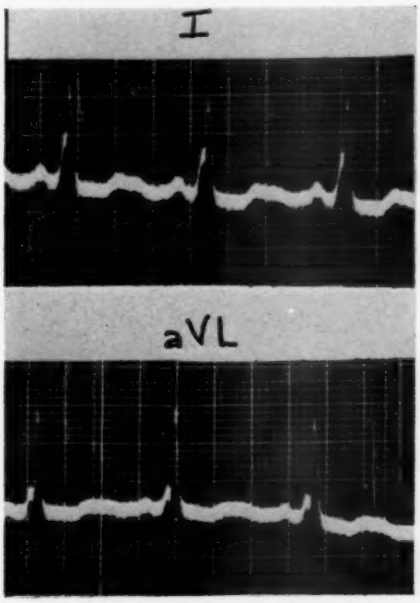


Fig. 10—WPW syndrome beat with a normal P-R interval. Note position of the delta wave in Lead I and in Lead aV$_L$. The position of the delta wave on the tracing depends on the position of the electrode in relation to the underlying structure.

sinus. Variability of structure in the same strip is a function of fusion beats. Another characteristic is the fact that the slur of the upstroke is usually all along the upstroke, rather than confined to its beginning, as it is in the WPW syndrome beat. In none of the tracings secured in various positions of this case was there any observation of a demarcated delta wave, or of a dislocation of the slur down-

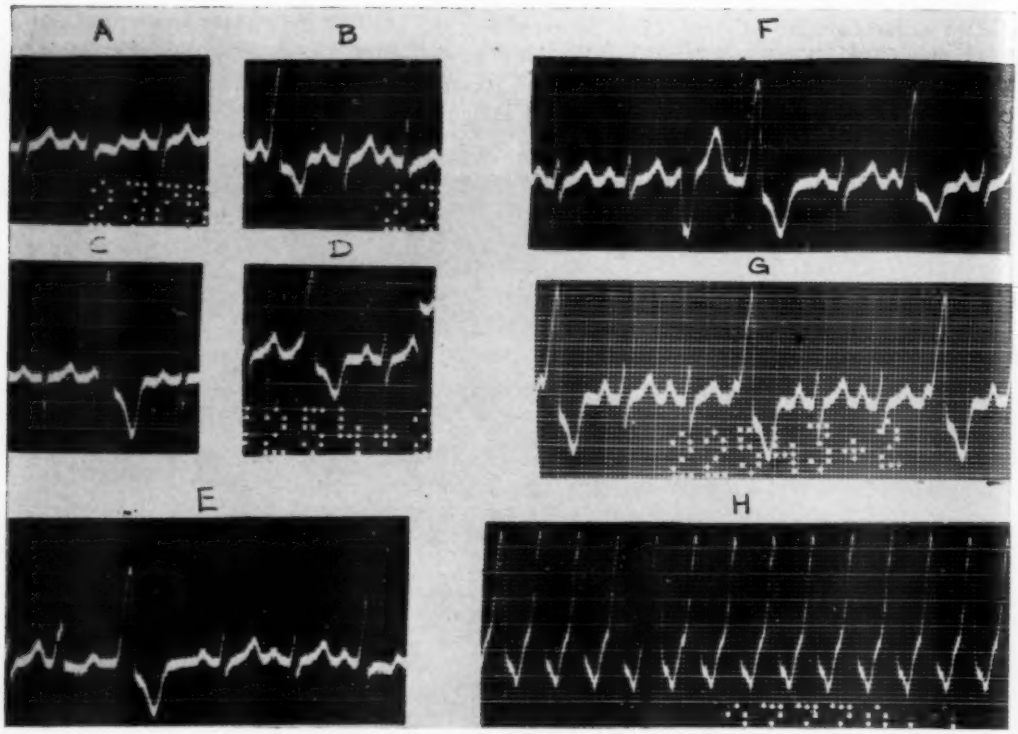


Fig. 11.—(W.E.) Lead II in all sections. Note in *B*, slur all along upstroke of QRS. Note absence of definite delta wave in *C*, and absence of P wave in *D* and *E*. *F* presents multifocal ectopic beats. In *G*—a section of a long strip—independent rhythmicity of the ectopic focus is illustrated. *H* is a strip of a long tracing depicting a ventricular tachycardia.

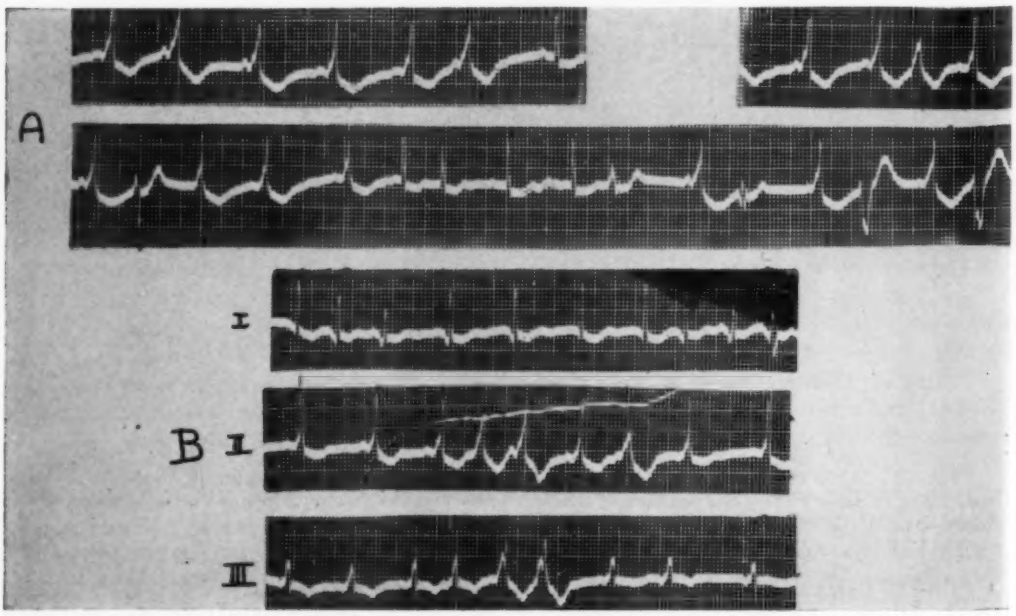


Fig. 12.—A tracing of an 84-year-old woman with a WPW syndrome, illustrating the type and origins of various arrhythmias. (See text for detailed description.)

ward. This patient was observed for many months. With the occasional exception of a bifocal ectopic beat, the fusion beats seemed to have originated in the same focus; and, in many instances, long strips of what is depicted in Fig. 11*G* (trigeminal rhythm) were secured. What accounts for this timing of the ectopic beat in relation to the sinus stimulus? It is reasonable to assume that the ectopic ventricular focus is so irritable as to discharge upon the slightest provocation, such as might be supplied by the mechanics of the auricular contraction. This accentuated irritability of the ectopic focus in the fusion beat makes it prone to initiate a ventricular tachycardia upon only modest provocation. Fig. 11,*H* represents just such an occurrence, which apparently resulted from an attempt to abolish the ectopic focus, in this case with a small dose of quinidine (0.8 Gm. in 6 hours). It was sufficient for the ventricular myocardium to be only slightly depressed by quinidine for the ectopic focus to assume control.

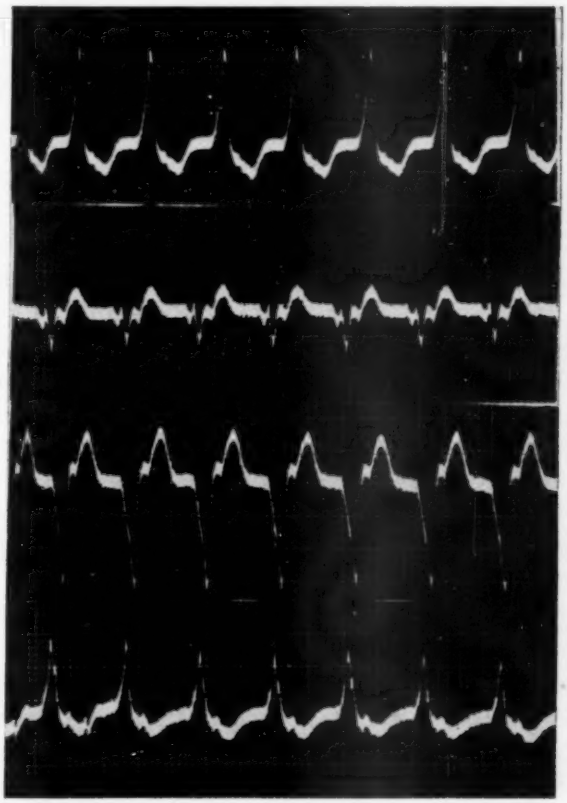


Fig. 13.—An ectopic tachycardia probably originating in the accessory conduction pathway. The structure following the QRS probably represents retrograde stimulations of auricular muscle.

The effect of quinidine upon the WPW syndrome is different. It depresses the aberrant pathway and permits the normal sinus pacemaker to inscribe a normal QRS complex, with one exception, however. In the presence of auriculoventricular block in the WPW syndrome, quinidine may produce a ventricular tachycardia. In a previous communication,[4] such an effect was demonstrated to take place with pronestyl.

Arrhythmias.—The subject of arrhythmias in the WPW syndrome is somewhat controversial. Some say that all arrhythmias are auricular in origin, but at times the aberrant pathway so deforms the predominant ectopic beat as to make it look ventricular in origin. Fig. 12 presents evidence of multifocal origin of ectopic beats in the WPW syndrome. Fig. 12,*A* presents sections of a long strip of Lead II. The upper left section shows a sinus arrhythmia with WPW syndrome

beats. The last beat of the section is a normal sinus cycle. The upper right section shows what appears to be an ectopic beat originating in the accessory pathway below its auricular projection. There is no P wave in this beat. Its structure resembles the adjacent complexes. It is wider, which is to be expected, since it is not a fusion beat of the impulse passing down the A-V node and the one transmitted down the accessory pathway. The lower section of Fig. 12,*A* presents, in addition to nodal and ventricular ectopic beats, some auricular ectopic beats. Hence, an auricular tachycardia is a potentiality in this case. The same phenomenon is seen in Lead I of Fig. 12,*B*. The fourth beat in Lead II looks again like an ectopic beat, originating in the accessory conduction system, and in Lead III two such beats occur in sequence—a threat of a paroxysm of ventricular tachycardia. Thus the WPW syndrome has the potentialities of presenting tachycardias of auricular, ventricular, and conduction system origins—both normal and accessory.

Fig. 13 presents a tachycardia due to an ectopic focus in the accessory pathway. The beats have the characteristic contour of the WPW syndrome beat, but no P wave is discernible. The small downward deflection preceding the QS in Lead II is possibly the delta wave as depicted in Figs. 2,*B* and 4,*D*. This tracing resembles Figure 5B in the paper by Pick and Katz,[5] and is another example of inherent rhythmicity of the accessory pathway.

COMMENT

In many respects, this paper is a sequel to the one recently published on the subject by Pick and Katz.[5] Apparently, it contains the "missing links" as does their paper, proving the existence of an accessory pathway in cases with WPW syndrome. By the "missing links" Pick and Katz understand the evidence that there are cases of WPW syndrome presenting "delayed anomalous conduction" and that "stimuli may originate in the anomalous pathway." Some other observations were incorporated in this report elucidating the variability of the duration of the QRS complex, as well as the length of the P-R interval. It was demonstrated that all the definition of WPW syndrome requires is the presence of a delta wave. This realization will tend to improve the diagnostic index in cases of aberrant A-V conduction—a matter of more than simple academic importance.

The lability of the RS-T segment was demonstrated. Apparently its orientation is not a function of the amplitude of the QRS complex as postulated by some observers.[6] While it is true that with clockwise rotation the amplitude of QRS-I would diminish and the direction and the T wave might be reversed—changes in the RS-T segment can occur spontaneously. Perhaps vagus tone is a factor. Cases with WPW syndromes are notoriously vagotonic. It is to be emphasized that axially there is nothing in common between the basic (normal) tracing and the WPW syndrome tracing in the same case, and their segmental abnormalities do not run in a parallel fashion. The RS-T deviation in the WPW syndrome is usually stereotyped. If an unusual deviation in direction or degree is observed, the reason for it should be looked for. Such deviations may occasionally signify myocardial damage, even if the basic tracing does not contain such information. By analogy, one should recall that in an occasional case of acute myocardial infarction the contour of an ectopic beat may suggest the diagnosis, rather than the configuration of the normal sinus complex.

The changes in the electrocardiogram that occur with change of position of the patient acquire a special interest in cases with WPW syndrome. In some cases, a concealed delta wave may appear, which makes a certainty of a diagnostic suspicion. The position of the electrode in relation to the accessory bundle is

what accounts for this phenomenon. This fact, incidentally, explains why the WPW syndrome configuration is frequently apparent in only one lead (usually Lead I), while the rest of the leads conform, more or less, to characteristics of a normal sinus beat.

SUMMARY

A selective number of electrocardiographic events occurring in cases of aberrant atrioventricular conduction (Wolff-Parkinson-White syndrome) are illustrated, and their significance briefly commented upon. The probability of an accessory conduction pathway between the auricles and ventricles is emphasized, and attention is drawn to some of the properties of this specialized conduction tissue. It is also pointed out that "vagotonia" is an essential attribute of the WPW syndrome, and is an important component in the electrocardiographic, as well as clinical, manifestations of cases with aberrant atrioventricular conduction.

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THE EVALUATION OF Q $_{aV_F}$ BY THE INITIAL SAGITTAL QRS VECTORS IN 70 AUTOPSIED CASES

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SINCE the introduction by Pardee[1] of the diagnostic significance of the Q wave in Lead III, various refinements in the criteria for the diagnosis of posterior myocardial infarction have been proposed.[2] Regardless of the criteria used, the electrocardiographic diagnosis of posterior myocardial infarction is still often difficult. The stricter the electrocardiographic criteria for the diagnosis of posterior myocardial infarction are, the more cases are excluded; while the broader the criteria become, the more cases are incorrectly diagnosed as having a posterior myocardial infarction. In the presence of a healed lesion the electrocardiographic residuals may be no more than tiny Q waves in Leads III and aV_F. On the other hand, occasional cases are seen with promient Q waves in Leads III and aV_F, but with no evidence of posterior infarction at autopsy. The differentiation of these two groups of cases is the main problem in the evaluation of Q waves in these leads. For example, 5 of our 25 autopsied cases with posterior infarction failed to show either a Q $_{aV_F}$ longer than 0.04 second or a Q $_{aV_F}$ greater than 25 per cent of R $_{aV_F}$. On the other hand, in our group of 45 autopsied cases without a posterior myocardial infarction, but with a Q wave in aV_F, 2 of the 45 had a Q $_{aV_F}$ longer than 0.04 second and 10 cases had a Q $_{aV_F}$ greater than 25 per cent of R $_{aV_F}$.

For these reasons, various efforts have been made to establish other, more accurate criteria for the diagnosis of posterior myocardial infarction than can be achieved by the use of the limb leads alone. One such approach is the use of unipolar leads posterior to the heart, either on the back or in the esophagus.[3-6] Back leads have been relatively unsuccessful and esophageal leads are inconvenient, particularly in sick patients. Another approach is vectorcardiography. Employing the Wilson tetrahedron, Milnor and co-workers[7] were invariably able to distinguish the Q wave in Lead III in subjects with no evidence of heart disease from the Q wave in Lead III in patients who had a definite clinical myocardial infarction. They found that this separation could be made on the basis of the initial vector of the sagittal loop inscribed during the first 0.012 second of ventricular depolarization. The initial QRS vector in cases without an infarct had an anterior direction (+5° to −62°), while those with an infarct had an upward direction (−68° to −97°).

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This report is an evaluation of the Q $_{aV_F}$ in 70 autopsied cases, 25 with and 45 without posterior infarction. The vectorcardiographic approach of Milnor and co-workers[7] was applied in this evaluation.

MATERIALS AND METHODS

For the past two years, all patients reporting to our heart station whose routine electrocardiograms showed a Q wave in Lead aVF were evaluated by constructing sagittal vectors. This was done by detaching the patient cable from the direct-writing machine and attaching it to a Sanborn Twin-Beam Electrocardiograph. The chest lead electrode was placed just to the left of the seventh thoracic vertebra. Lead aVF and the V lead from the back (V_B) were then recorded simultaneously at a paper speed of 75 mm. per second, employing a standardization of 10 mm. per millivolt in each lead. The sagittal vectors at 0.01 and 0.02 second were constructed by measuring the deflection at these intervals in each lead and using these measurements as the tangent of the angle of the vector. Although this could be done fairly accurately by direct inspection, for the purpose of this study the measurements were made by projecting the simultaneous aVF and V_B electrocardiograms onto a large screen. The sagittal vectorcardiogram constructed in this fashion varied from the Wilson tetrahedrons employed by Milnor and associates[7] and Conway and associates[8] only in standardization, and in that the construction was done by manual rather than electronic methods. The duration of the Q wave measured from its onset to its return to the isoelectric line and the amplitude of the Q and R waves in Lead aVF were also measured. Cases with left bundle branch block were excluded.

Of more than a thousand patients in whom these leads were taken, 70 died and were autopsied. Those with an infarction of the diaphragmatic or posterior wall of the left ventricle made up the group of 25 cases classified as having a posterior myocardial infarction. The 45 remaining cases included 22 with neither infarction nor myocardial fibrosis, 18 with myocardial fibrosis, and 5 with an infarct other than posterior. The electrocardiographic and sagittal vector data were correlated with the autopsy data.

RESULTS

Correlation of the autopsy data and the sagittal vectors at 0.01 and 0.02 second revealed a better separation of cases with and without a posterior myocardial infarction when the 0.02 second vector was used. The values recorded at 0.01 second were therefore not used. The range of 0.02 second vectors from $-65°$ to $-150°$ included most of the posterior infarcts with the fewest false positives. Therefore, all 0.02 second sagittal vectors falling in this range were classified as positive for posterior myocardial infarction, while all of the others were classified as negative (Fig. 1). Representative records with a positive 0.02 second vector and a negative one are shown in Fig. 2.

The electrocardiographic and sagittal vector data are presented in Table I. It can be seen that the major limitation of a Q $_{aV_F}$ 0.04 second or longer in duration as a criterion of posterior myocardial infarction in the large number of false negatives, 10 of 25 cases with a posterior infarct having a Q $_{aV_F}$ less than 0.04 second in duration. The criterion of a Q $_{aV_F}$ greater than 25 per cent of R $_{aV_F}$ is even less accurate, having 10 false positives among 45 cases without posterior infarction, and 6 false negatives among the 25 cases with posterior infarction. If both of these criteria are required for the diagnosis of a posterior infarction, a case with only one of them being classified as probably having a posterior infarction, 7 cases are still completely misdiagnosed. Of these 7, there are 2 false positives and 5 false negatives. Furthermore, of the 13 cases classified as a probable posterior infarction, 8 had no posterior infarction at autopsy.

The 0.02 second sagittal vector had a greater accuracy in the diagnosis of posterior infarction, being correct in 62 of the 70 cases. However, since there were 7 cases with a false positive 0.02 second sagittal vector, the data were evaluated in terms of a combination of a positive vector and a Q aV_F 0.04 second or longer in duration. When both of these criteria are required for the diagnosis of posterior myocardial infarction and the presence of one of these criteria is interpreted as evidence of a probable posterior infarct, false positives and false negatives are completely eliminated and 11 of the 18 classified as having a probable posterior infarct had one at autopsy.

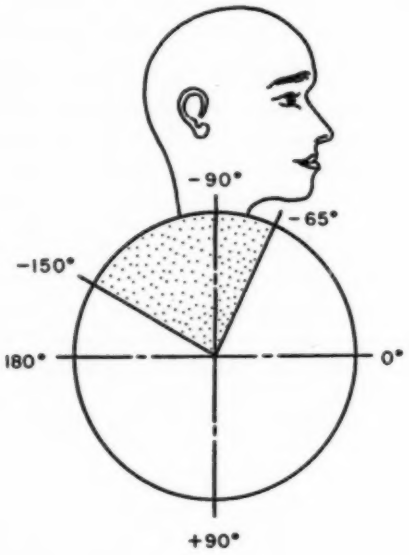

Fig. 1.—Classification of 0.02 second sagittal vectors. All vectors falling between −65° and −150° are classified as positive. All other are classified as negative.

Therefore, when the combination of a positive 0.02 second sagittal vector and a 0.04 second or longer Q aV_F was used for the diagnosis of posterior myocardial infarction, a correct diagnosis was made in 90 per cent of the 70 cases. The remaining 10 per cent were classified by these criteria as probably having a posterior infarct, none being found at autopsy. There were no cases that were completely misdiagnosed. In comparison, using the criteria of a Q aV_F equal to or greater than 0.04 second and a Q aV_F greater than 25 per cent of R aV_F there was a correct diagnosis in 78 per cent; a probable posterior infarct was diagnosed in 12 per cent in which none was found at autopsy; and 10 per cent of the cases were misdiagnosed.

DISCUSSION

The observations reported here, like those of many others, showed that it is impossible to separate completely by the electrocardiogram cases with posterior myocardial infarction from those without it. Of the electrocardiographic criteria studied, the presence of a Q wave in Lead aV_F 0.04 second or over in duration

was the most useful, correctly indicating a posterior infarct in 15 out of 17 cases. Its absence was much less significant.

The use of the 0.02 second sagittal vector as a criterion for the diagnosis of a posterior myocardial infarction was more accurate than the electrocardiographic criteria in this group of cases. A positive 0.02 second sagittal vector was present in 24 of 25 cases with posterior infarction at autopsy, while 38 of 39 cases with a negative sagittal vector had no posterior infarct at autopsy. The presence of the 7 false positives was the most serious limitation of the sagittal vector. However, some of these 7 cases might have been electrocardiographically equiva-

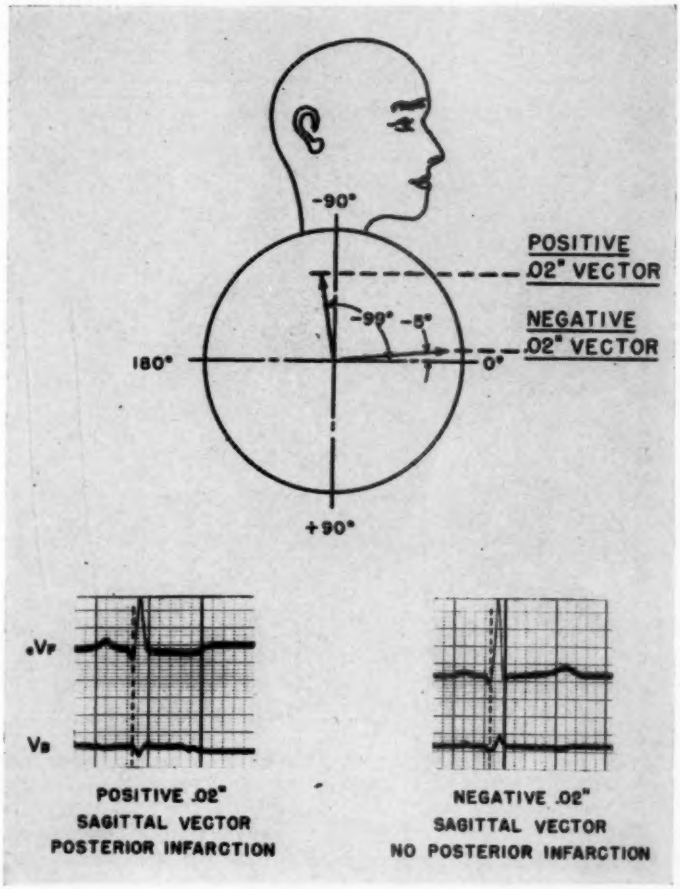

Fig. 2.—Representative examples of simultaneous tracings of Leads aV_F and V_B in cases with and without a posterior myocardial infarction. The leads are recorded at 75 mm. per second with a standardization of 10 mm. per millivolt. The 0.02 second sagittal vectors constructed in each case are shown.

lent to a posterior infarction, as 3 had diffuse fibrosis localized to the posterior wall of the left ventricle, and one had a septal infarct.

Examination of the sagittal vectors reveals the basis for the failure in diagnosing posterior myocardial infarction by means of unipolar back leads. It has been assumed that Q waves would be present in back leads in posterior infarction just

TABLE I. EVALUATION OF THE ACCURACY OF CRITERIA USED IN THE DIAGNOSIS OF POSTERIOR MYOCARDIAL INFARCTION (P.M.I.) IN 70 AUTOPSIED CASES, 25 WITH AND 45 WITHOUT A P.M.I.

	CRITERIA FOR THE PRESENCE OF A P.M.I.			CRITERIA FOR A PROBABLE P.M.I.			CRITERIA FOR THE ABSENCE OF A P.M.I.		
		TRUE POSITIVE	FALSE POSITIVE		DID HAVE P.M.I.	DID NOT HAVE P.M.I.		TRUE NEGATIVE	FALSE NEGATIVE
Lead aV_F	Q aV_F > .04″	15	2	—			Q aV_F < .04″	43	10
	Q aV_F > 25% R aV_F	19	10	—			Q aV_F < 25% R aV_F	35	6
	Q aV_F > .04″ and Q aV_F > 25% R aV_F	15	2	Either Q aV_F > .04″ or Q aV_F > 25% R aV_F	5	8	Q aV_F < .04″ and Q aV_F < 25% R aV_F	35	5
.02″ sagittal vector and Lead aV_F	.02″ sagittal vector of −65° to −150°	24	7	—			.02″ sagittal vector not −65° to −150°	38	1
	.02″ sagittal vector of −65° to −150° and Q aV_F > .04″	14	0	Either .02″ sagittal vector of −65° to −150° or Q aV_F > .04″	11	7	.02″ sagittal vector not −65° to −150° and Q aV_F < .04″	38	0

as they are in precordial leads in anterior infarction. In our group of 25 patients with posterior infarction, however, 17 had a 0.02 second sagittal vector directed toward the back with an R wave in the back lead at this time. This is illustrated in Fig. 3 where an R wave in V_B is present with a typical posterior myocardial infarction. It is interesting to note that regardless of cardiac position a Q wave

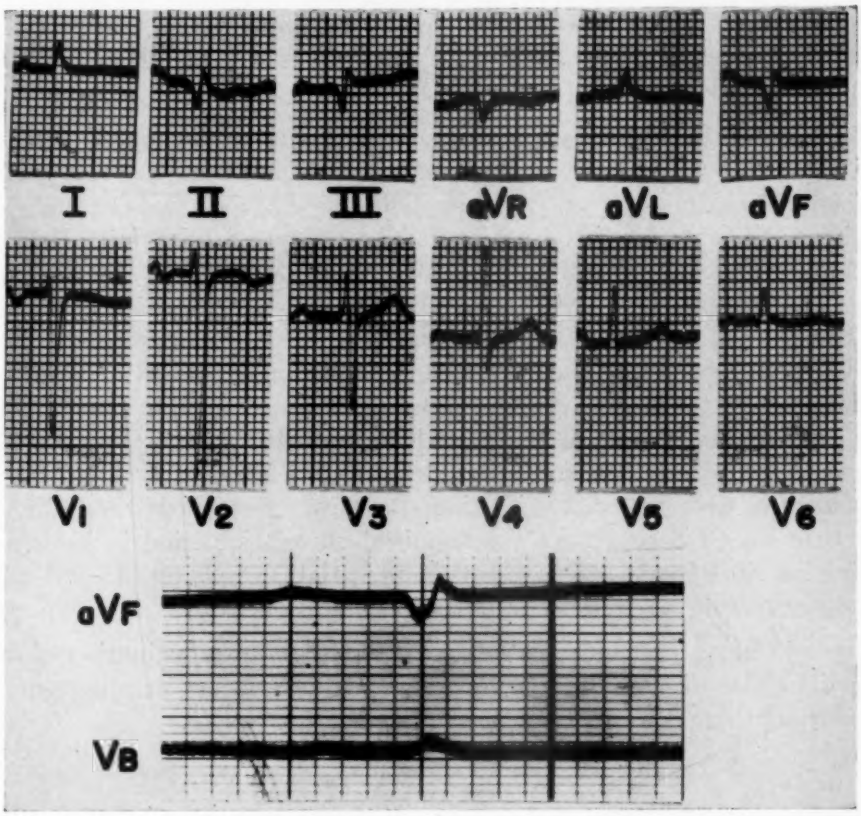

Fig. 3.—The electrocardiogram and simultaneously recorded Leads aV_F and V_B of a patient with a posterior myocardial infarction confirmed at autopsy. The initial R wave in V_B can be seen.

was found in the mid-back lead in almost all of the 103 normal men studied by Simonson.[9] There are a number of reasons for the failure to find Q waves in the back leads in cases of posterior myocardial infarction. In the first place, most so-called posterior infarctions are predominately inferior. In the second place, body distortion is great on the chest-back (Z) axis, as has been shown by Schmitt and Simonson with torso model experiments.[10] This same distortion was present in our calculated sagittal vector, and it is probable that diagnostic criteria would have been much more precise if an orthogonal lead system had been used. An increased diagnostic accuracy was obtained by the use of a back lead in this study because it was used to determine sagittal vectors, rather than as a unipolar lead in a search for Q waves.

The failure to achieve the sharp dichotomy obtained by Milnor and associates[7] is probably due to the entirely different method of case selection. Their cases were all living patients, while ours had all been autopsied. Their group without posterior infarction was made up of individuals whose cardiovascular systems were clinically normal, while our group of autopsied cases without posterior infarction contained many individuals with myocardial fibrosis, or infarcts in other areas. Furthermore, Burch and his associates[11] stated there was considerable variation in the upward direction of the initial vectors in their cases of posterior infarction. However, they did not present data on the initial sagittal vectors in these cases.

There is a sufficiently increased accuracy in the evaluation of Q waves in Lead aV_F to recommend the routine use of the 0.02 second sagittal vector for this purpose. This vector can easily be determined with a two-channel electrocardiograph. The angle of the vector can be estimated with fair accuracy by inspection alone. If a two-channel electrocardiograph is not available for recording V_B simultaneously with aV_F, an estimate of the 0.02 second sagittal vector can be made in most cases by recording these leads separately. The estimated vector will be more accurate where the duration of the QRS complex is the same in both leads, diminishing the chance of phase errors. In cases where the QRS $_{aV_F}$ and V_B are of equal duration, an R $_{V_B}$ associated with a Q $_{aV_F}$ would suggest a posterior infarction in most instances, while a large Q $_{V_B}$ would rarely be present in cases with posterior infarction. In most cases where the QRS $_{V_B}$ was shorter than the QRS $_{aV_F}$, there was an initial isoelectric period in V_B while a Q was being inscribed in aV_F. This results in an initial QRS vector of $-90°$, which is highly suggestive of the presence of posterior infarction.

Although not a part of this study, it is likely that an evaluation of sagittal vectors would be of value in the diagnosis of posterior myocardial infarction in cases where there is a small R wave in Leads III and aV_F.

SUMMARY

The 0.02 second sagittal vector is more accurate in the diagnosis of posterior myocardial infarction than the usual electrocardiographic criteria. This conclusion is based on a study of 70 autopsied cases with a Q wave in Lead aV_F in which a sagittal vector was determined. A positive 0.02 second sagittal vector (one from $-65°$ to $-150°$) was present in 24 of 25 cases with posterior infarction, while 38 of 39 cases without a posterior infarction had a negative 0.02 second sagittal vector. When both a positive 0.02 second sagittal vector and a Q $_{aV_F}$ 0.04 second or longer were required for the diagnosis of posterior infarction, and the presence of only one of these two criteria was interpreted as probably indicating a posterior infarction, 90 per cent of these 70 cases were correctly diagnosed. The remaining 10 per cent were cases diagnosed as probably having a posterior myocardial infarction when none was present at autopsy. There were no cases completely misdiagnosed by these criteria, while 10 per cent of cases were misdiagnosed when only the depth and duration of Q $_{aV_F}$ were used.

The 0.02 second sagittal vector can be determined easily by the use of a two-channel electrocardiograph and can be estimated in most cases by the separate recording of aV_F and the Wilson V_B lead.

We are grateful to Ralph E. Glaze, Isaiah Dixon, Esther Sadoff, and Suzanne Warner for help in collecting the material in this paper.

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Clinical Reports

COMPLETE PULMONARY VENOUS DRAINAGE INTO THE PORTAL VEIN WITH MULTIPLE CONGENITAL ANOMALIES

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ANOMALOUS drainage of all or part of the pulmonary veins is an uncommon finding. One of the rarest of these anomalies is complete drainage of all pulmonary veins into the portal vein.

In 1942, Brody[15] collected from the literature, including his own, 106 cases of anomalous pulmonary drainage, 38 of which were completely anomalous, Young[19] brought the total number of cases to 128 in 1947, when he reported his case and summarized the cases reported since Brody's article as well as those not mentioned by Brody. Attention was drawn by Edwards and Du Shane[9] in 1950, to a case of complete portal drainage of the pulmonary veins which Hu[5] had reported in 1929. In 1952, Healy[4] tabulated 147 cases of anomalies of the pulmonary veins, most of which had been mentioned by Brody, Young, or Du Shane and Edwards. According to this tabulation, up to 1952, there were 9 cases of complete and one of partial pulmonary venous drainage to the portal vein reported in the literature. Weinberg,[24] whose report was not referred to by Healy, published a case of complete pulmonary venous drainage into the portal vein. An additional case of complete pulmonary venous drainage into the portal vein is reported in this paper, thus bringing to eleven the total number of cases with completely anomalous pulmonary drainage into the portal vein.

CASE REPORT

A full-term white female infant, weighing 4 pounds, 12 ounces, was born after an uneventful pregnancy and a spontaneous labor and delivery. The mother had given birth to a 7 pound, 13 ounce normal full-term male infant five years previous to the birth of this baby. This pregnancy and labor were also uneventful. The mother had never had any illnesses other than the usual childhood diseases. The pediatrician had known the child's mother from childhood, and had known the members of the father's and mother's families. To the pediatrician's knowledge there was no history of any previous congenital abnormalities.

Upon initial examination by a pediatrician the child was found to have a double cleft palate, an imperforate anus, multiple ectodermal defects, bilateral microphthalmus, webbing of the left

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axilla, absence of finger- and toenails, talipes varus of the right foot, a short fifth digit of both hands with only a rudiment of a distal phalanx, and a questionable hydrocephalus. The baby lived for four days, during which she took no food and was "rigid" most of the time. Her condition was considered poor from birth and she was frequently cyanotic. During the four days of life, her respiration became more irregular and her pulse weaker. She became generally edematous and finally died of respiratory arrest.

The infant was embalmed in the routine manner in which cadavers are prepared for dissection. At necropsy, the infant, measuring 0.329 meter from crown to rump, was found upon preliminary examination to have bilateral microphthalmos, talipes varus of the right foot, absence of toe- and fingernails, imperforate anus, a double cleft palate, and short fifth digits of both hands. Dissection of both right extremities revealed no anomalies. The right hand and foot and both left extremities were not dissected.

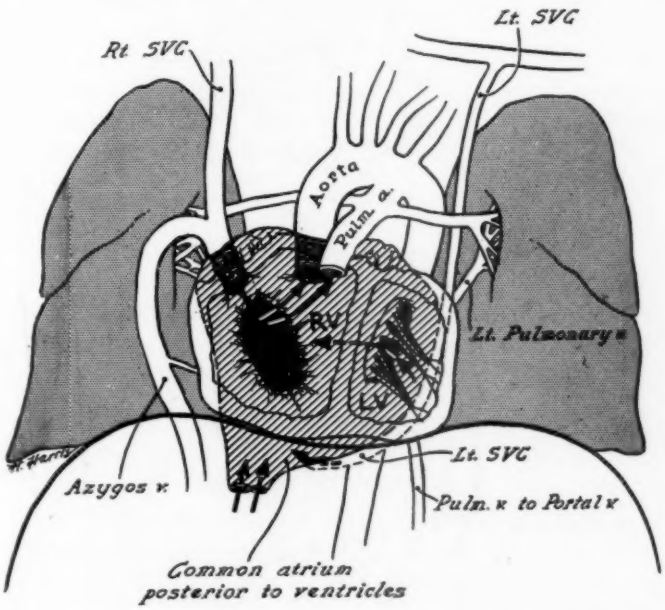

Fig. 1.—Diagram of cardiac and great vessel anomalies responsible for the infant's death at 4 days. See text.

The circumference (fronto-occipital) of the head was 35 cm. The calvarium was opened and it was noted that the right cerebral hemisphere was larger than the left, as 3 is greater than 2. There was no corpus callosum. There was an internal hydrocephalus down to the level of the aqueduct of Sylvius where the ventricular system was atretic. The topical markings of the brain were normal, as were the intracranial vessels. Although the face and neck were not extensively dissected, it was noted that the great vessels were in their usual anatomical relationships at the base of the neck.

The cardiovascular system was completely anomalous. There was a common triangular-shaped atrium with two appendages (right and left) coming over the superior aspect of the ventricles which were anterior to the atrium. This atrium received blood from the right superior vena cava at the right superior angle, from the two hepatic veins at the inferior angle, and from the persistent left superior vena cava which ran in the left atrial wall to the inferior angle where it opened just to the left of the hepatic veins. There was no evidence of an interatrial septum. There were two ventricles which were connected to the atrium. The valve around the left atrioventricular orifice leading to the left ventricle was a single leaf on the medial side of the orifice with its chordae crossing over to the lateral wall of the ventricle. The left ventricle had no

communications with either the pulmonary or systemic circulation, and any blood which entered from the atrium therefore had to return to the atrium and then pass through the right ventricle to be circulated through the arterial systems. The atrium communicated with the right ventricle via an atrioventricular orifice which was surrounded by a circular valve whose chordae were attached to the anterior ventricular wall. The blood from the right ventricle was pumped out into the aorta and pulmonary artery which were connected by a patent ductus arteriosus (Fig. 1).

The blood from the lungs, which had no lobar markings, was collected by three main pulmonary veins on the right and one pulmonary vein on the left. These veins joined in the midline at the inferior border of the heart to form one common vein which passed through the esophageal

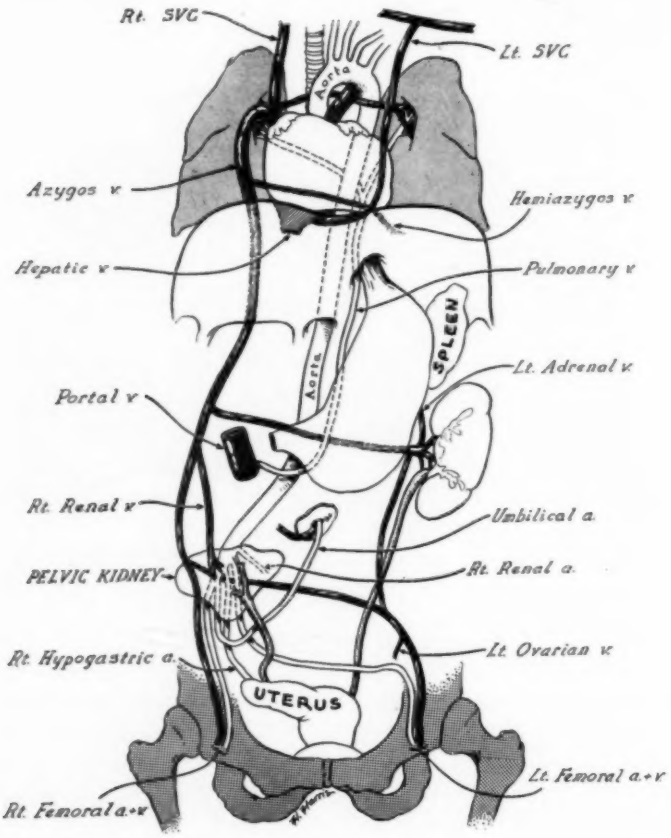

Fig. 2.—Diagram illustrating additional anomalies of circulation, such as the inferior vena cava. See text.

hiatus of the diaphragm anterior to the esophagus. In the abdomen this common pulmonary venous trunk followed the lesser curvature of the stomach to the pylorus where it passed behind the stomach to join the portal vein which crossed the anterior surface of the pyloric-duodenal junction to enter the liver normally. The tributaries of the portal vein, other than the anomalous pulmonary drainage, were normal.

The aorta was normal until it reached the level of the renal arteries, at which point it swung to the right midway between the spine and the lateral wall of the abdomen. The right renal artery came off of the aorta where the aorta passed behind the kidney on the brim of the pelvis. The left renal artery to the normally placed left kidney came off the aorta at the level of the celiac

axis. Behind the right kidney the aorta divided into several branches: (1) a vessel which continued as the right external iliac; (2) a right umbilical artery; (3) a right hypogastric artery; and (4) an artery which passed down into the pelvis behind the sigmoid colon, up the left lateral side of the pelvis, and out the femoral canal as the left femoral artery. The pelvic ramifications of these arteries were too small to be traced out in the fixed specimen. There was no left umbilical artery. (Fig. 2.)

The veins draining the pelvic structures, the lower extremities, and the right kidney all joined behind the right kidney to form an anomalous inferior vena cava which lay lateral to the aorta. This vessel passed up the right lateral gutter of the abdomen and through its own hiatus in the diaphragm to become continuous with the azygous vein which emptied into the right superior vena cava. The azygous vein also received the blood from the hemiazygous vein which crossed the midline at the level of the seventh thoracic vertebra. The persistent left superior vena cava received the veins from the upper part of the left thoracic cage and the left upper extremity. (Fig. 2.)

The liver, gall bladder, spleen, and pancreas were grossly normal. The gastrointestinal tract was also normal except for a greatly dilated rectum and sigmoid colon and an imperforate anus with the rectum forming a blind pouch 5 mm. from the skin. The urinary tract was grossly normal except for the right pelvic kidney and marked lobulation of both kidneys. The ovaries, their ligaments, and their vessels were normal. The uterus had a large right horn. Otherwise, the reproductive tract was normal.

DISCUSSION

The embryology of the pulmonary veins has been extensively studied by Edwards[23] and others[18,20] and will not be discussed at this time.

The knowledge of the presence of anomalous pulmonary venous drainage is becoming increasingly important because of the frequency of intrathoracic operations. The surgeon may be saved surgical difficulties and postoperative morbidity (and possibly mortality), if he is aware preoperatively of the presence of anomalies of the pulmonary veins.

The diagnosis of these anomalies is also important from the standpoint of definitive treatment since, as Hughes and Rumore[16] stated, "Anomalous drainage of greater than 50 per cent of the lungs is not compatible with life to adulthood."

Many authors have published articles in the last four to five years relating to the diagnosis of anomalous pulmonary drainage during life. Keith,[25] Grishman,[11] Bruce,[22] Sepulveda,[26] Knutson,[27] and others[1,2,6] have recently presented the clinical features of anomalous drainage with reference to cardiac catheterization, angiocardiography and/or radiologic findings.

SUMMARY

A brief review of the literature pertaining to anomalous pulmonary venous drainage is presented.

A case of total pulmonary venous drainage into the portal vein associated with a trilocular heart whose left ventricle did not communicate with either the pulmonary or systemic circulation, a patent ductus arteriosus, an anomalous inferior vena cava continuous with the azygous vein, a persistent left superior vena cava, internal hydrocephalus, double cleft palate, a right pelvic kidney, an anomalous abdominal aorta, talipes varus of the right foot, an imperforate anus, and an anomalous uterus is presented.

I acknowledge the very helpful advice of Dr. Emile Holman, Professor of Surgery, Emeritus, Stanford University School of Medicine, and Dr. Thomas Algard, Assistant Professor of Anatomy, Stanford University School of Medicine. My thanks also go to Mrs. Cowles for the drawings contained in this paper.

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MYOCARDIAL TRAUMA PRODUCED BY NONPENETRATING CHEST INJURY

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INTRODUCTION

AUTOMOBILE accidents causing significant injury to human beings have become the most alarming statistics of trauma. But despite commendable perception of the associated "steering wheel" injury of the chest wall, with or without penetration of the thoracic cage, recognition of other, more subtle, modes of actual myocardial trauma has been either nonexistent or evidenced too infrequently.

Although the entity of the conventional anginal syndrome due to coronary artery atherosclerosis is universally acceptable without "objective" supportive data, the diagnosis of myocardial contusion due to whatever cause is subject to overly critical suspicion.

Having the temerity to present two such cases, in the absence of biopsy material or confirmation by autopsy findings, we detail subsequently our observations which lead us to conclude that these patients suffered recognizable, significant, and real injury of the myocardium in the absence of laceration, puncture, or gross distortion of the protective thoracic wall. Neither happened to be a victim of automotive units but each represents to the practitioner or diagnostician interested in lesions of the heart a clinical traumatic problem requiring careful assessment and cautious management.

CLASSIFICATION OF CARDIAC CASUALTIES

Cardiac injury would seem to fall into the following categories:

A. *Concussion.*—Altered intactness of the myocardium resulting from a nonpenetrating blow to the chest or from (uncontrolled) hurtling of the body.

B. *Contusion*‡.—Altered integrity of the myocardium, with or without swelling and/or ecchymosis, produced by nonlacerating injury to the chest wall. (1) Myocardial. (2) Coronary arterial tree.

C. *Compression.*—Compactness of the heart due to external pressure.

D. *Laceration.*—Tear of a portion of the heart. (1) Penetrating wound: (a) direct (by external object thrust into the precordium or diverted there); (b) indirect (rib fracture or sternal fracture). (2) Surgical catastrophe: (a) transection of coronary vessels during heart surgery, particularly mitral

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‡Category B prompts this report. Such lesions often have medicolegal implications, an aspect not primarily appreciated in the practice of clinical medicine.

valvular commissurotomy[11]; (b) perforation of cardiac chamber wall manually or by instrument. (c) catheterization of coronary sinus.

E. *Rupture.*—Perforation of a part of the heart. (1) Intrinsic (spontaneous): (a) myocardial necrosis due to infarction[15]; (b) endocardial disease (rupture of a diseased chorda or papillary muscle). (2) Extrinsic (body hurled through space): (a) great-vessel avulsion; (b) extrorsion of a valve.

Medical literature is documented with discussions of cardiac trauma secondary to nonpenetrating chest injuries.[1,2,3,6,7,10,13,16,17,19] Gore[8] recently has questioned the validity of many cases cited, on the grounds that heart disease unrecognized prior to the traumatic episode actually was the basis for the resultant cardiac illness.

Although we are accustomed to consider the brain, liver, spleen, and kidneys as susceptible to concussion, contusion, laceration, or compression, the possibility of such lesions occurring in the heart is frequently overlooked.[4,6,7]

Many of the reports in the literature emphasize that the physician must maintain a degree of suspicion to recognize the diagnosis, not only when there has been supposedly harmless chest-wall trauma but also when there has been extensive body injury. Such victims may present themselves to the physician promptly after injury or only after a lapsed period of hours or days.

A variety of symptoms may ensue. In the immediate posttraumatic period, if consciousness is not lost, the more frequent complaints are weakness, dizziness, near-syncope, dyspnea, and mild to severe retrosternal pain. After a latent period, cough, dyspnea, palpitation, anginal syndrome, or disturbances of cardiac rhythm may cause the individual to seek medical attention.[3,4,17]

CASE REPORTS

Two instances of cardiac trauma studied recently on the medical service of the Hahnemann Hospital are presented. Survey of the English-language literature did not emphasize that, under certain circumstances, cardiac trauma must be considered seriously in the differential diagnosis of an acute myocardial abnormality. Our first case illustrates the need for detailed history and aggressive pursuit of diagnosis.

CASE 1.—A 36-year-old white housewife was admitted to Hahnemann Hospital on the evening of May 20, 1955, complaining of chest pain and dyspnea of two days' duration. She stated that two days before, while scrubbing floors at home, she experienced sudden onset of severe, constricting, retrosternal pain which was knifelike in character. This lasted two or three minutes and was replaced by a less severe, precordial ache which radiated down her left arm, lasting approximately one hour. At the same time, she became short of breath and because of that was unable to lie down. The following evening, while attempting again to do housework, the severe dyspnea and constricting pain returned. With the onset of these symptoms, she was brought to the hospital by her son.

The woman denied previous episodes of chest pain, dyspnea, orthopnea, or progressive fatigability. There was no history of heart disease, hypertension, diabetes, rheumatic fever, diphtheria, or venereal disease.

Her only child, a delinquent son, 15 years old, had recently been released from a reformatory. The patient was separated from her husband, who was an inmate of a state penitentiary. Her father had died of hypertension at the age of 65; her 66-year-old mother suffered from heart disease (etiology unknown) and recently had had a "stroke."

On admission, the patient appeared overweight, weak, and somewhat lethargic. The chief complaint was severe retrosternal chest pain. Temperature was 99.6°F.; pulse, 110 per minute; respirations, 24 per minute; blood pressure, 116/70 mm. Hg.

Physical examination showed no neck vein distention. Definite tenderness without crepitation was found over the gladioloxyphoid junction. The chest wall bore no evidence of injury. Lung fields were clear to percussion but, on auscultation, fine right basilar râles were audible.

On examination of the heart, the point of maximum impulse was not palpable. Diastolic gallop rhythm was heard readily at the third intercostal space to the left of the sternum at the rate of 110 per minute. No murmurs or adventitious mediastinal sounds were detectible.

On examination the abdomen and extremities appeared normal. Femoral, dorsalis pedis, and posterior tibial pulses were normally pulsatile.

Hospital Course.—Laboratory data: Hemoglobin was 13.2 Gm., hematocrit, 42; corrected sedimentation rate (Wintrobe), 17 mm. per hour; white blood cells, 6,450 with a normal differential. Urinalysis was negative. Lee-White coagulation time was 9 minutes, 7 seconds. Prothrombin time was 100 per cent. Total cholesterol was 264 mg. per cent with 62 per cent esters; blood urea nitrogen, 8 mg. per cent; 2-hour postprandial blood sugar, 100 mg. per cent; Kolmer and VDRL, nonreactive.

Six days after admission, corrected sedimentation rate was 42 mm. per hour, with 5,600 white blood cells. The elevated sedimentation rate gradually returned to normal and on discharge was 15 mm. per hour.

A portable chest film taken shortly after admission demonstrated a heart of normal size, position, and configuration. No cardiopulmonary abnormalities were present.

The day following admission, the retrosternal ache and sternal tenderness persisted. This tenderness and the patient's age aroused our suspicions. Examination and laboratory studies revealed the patient was not hypertensive, diabetic, or polycythemic. Another important fact, emphasized recently by James,[9] was that the patient was premenopausal. We doubted, on grounds of probability, that she had coronary artery disease due to atherosclerosis. Signs suggesting coronary arterial embolism or coronary ostial occlusion were lacking. So we questioned her more specifically with regard to the possibility of anterior chest trauma. She admitted reluctantly that about twelve hours prior to the onset of her acute symptoms her 15-year-old, 200-pound son had struck her a forceful blow on the chest during a fit of anger.

Our patient's immediate treatment consisted of complete bed rest, oxygen via nasal catheter, and Demerol intramuscularly as needed for pain. Aqueous heparin and Dicumarol therapy were initiated shortly after admission. Both were discontinued when the history of trauma was elicited. Since traumatic myocardial ischemia is extrinsic in etiology, it is conceivable that the likelihood of hemopericardium is enhanced if anticoagulant therapy is used.

Gallop rhythm disappeared but sinus tachycardia from 110 to 130 per minute persisted for six days. During this period her temperature ranged between 99° and 100°F. orally and the fine right basilar râles persisted. One week after admission, temperature was normal, the cardiac rate was 88 per minute, her chest was physiologic, and the pain and tenderness had disappeared. After three weeks of bed rest, the patient was ambulated cautiously and discharged completely asymptomatic four weeks after admission. Fig. 1 depicts the accident ward electrocardiogram and serial tracings taken during her hospitalization.

CASE 2.—A 51-year-old white man was admitted to Hahnemann Hospital accident ward at 8:00 A.M. on Sept. 25, 1955, complaining of severe chest pain and extreme shortness of breath. The pain, noted by the patient approximately three hours prior to admission, woke him from his sleep. It was described as a "crushing" sensation centered over the entire anterior chest wall. On wakening, there had been no pain radiation, but one-half hour later the distress disseminated as a dull ache down both arms and up to the neck and jaw. To reach the hospital, this man walked eight blocks, taking approximately three hours to do so because of extreme pain and dyspnea associated with the effort.

On admission, blood pressure was 160/82 mm. Hg, pulse thready at 160 per minute, and respirations 32 per minute. A combination of fine and coarse râles were audible over the entire lower half of the thorax. His marked pallor and profuse diaphoresis supported the inference of clinical shock. Digitalization was accomplished rapidly with 1.6 mg. Cedilanid intravenously.

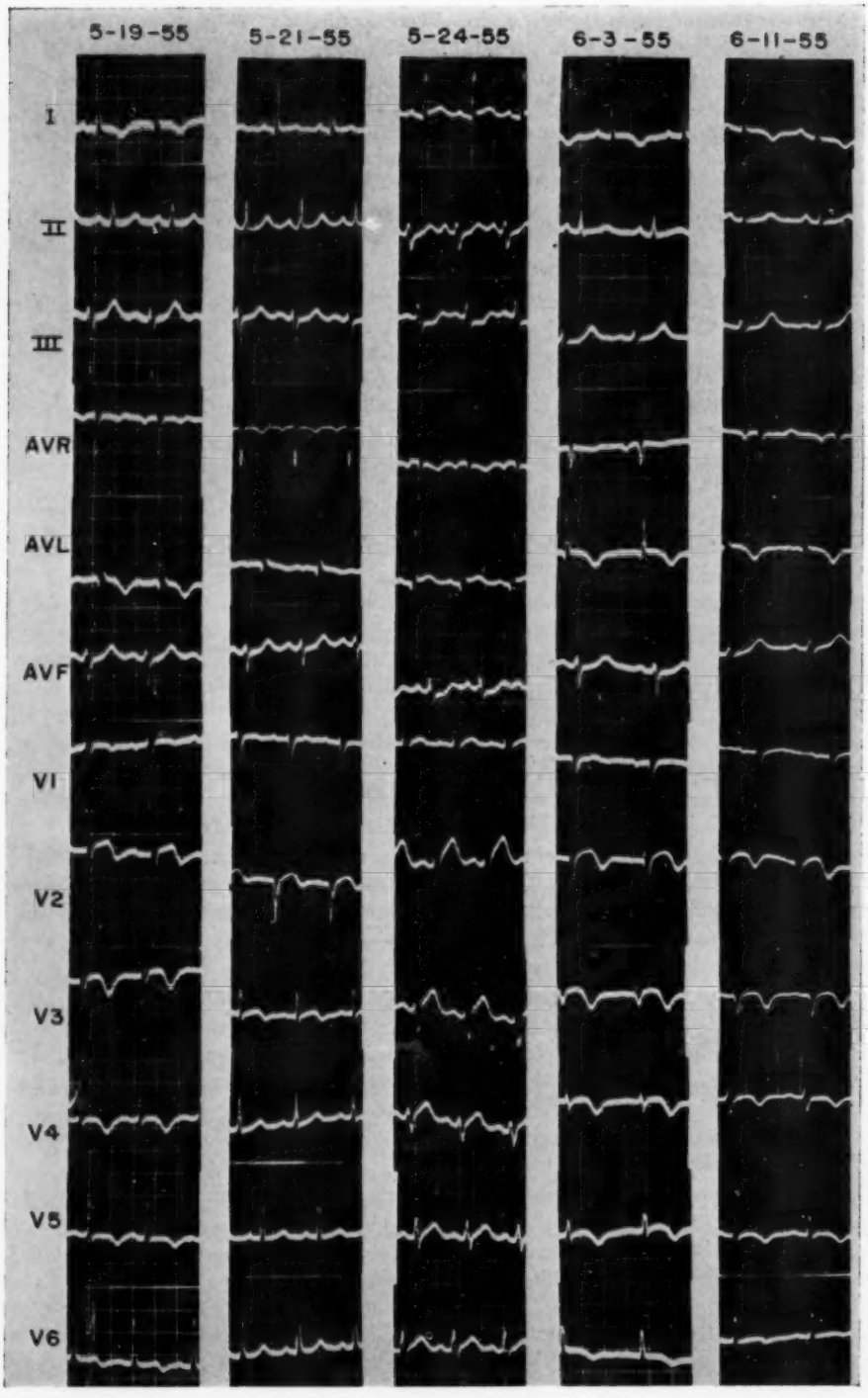

Fig. 1.—Serial ECG study of 36-year-old white woman suffering myocardial lesion produced by nonpenetrating chest injury, a forceful punch. Note especially the S-T segment and T-wave changes in Leads I, aV$_L$, and the unipolar precordial leads.

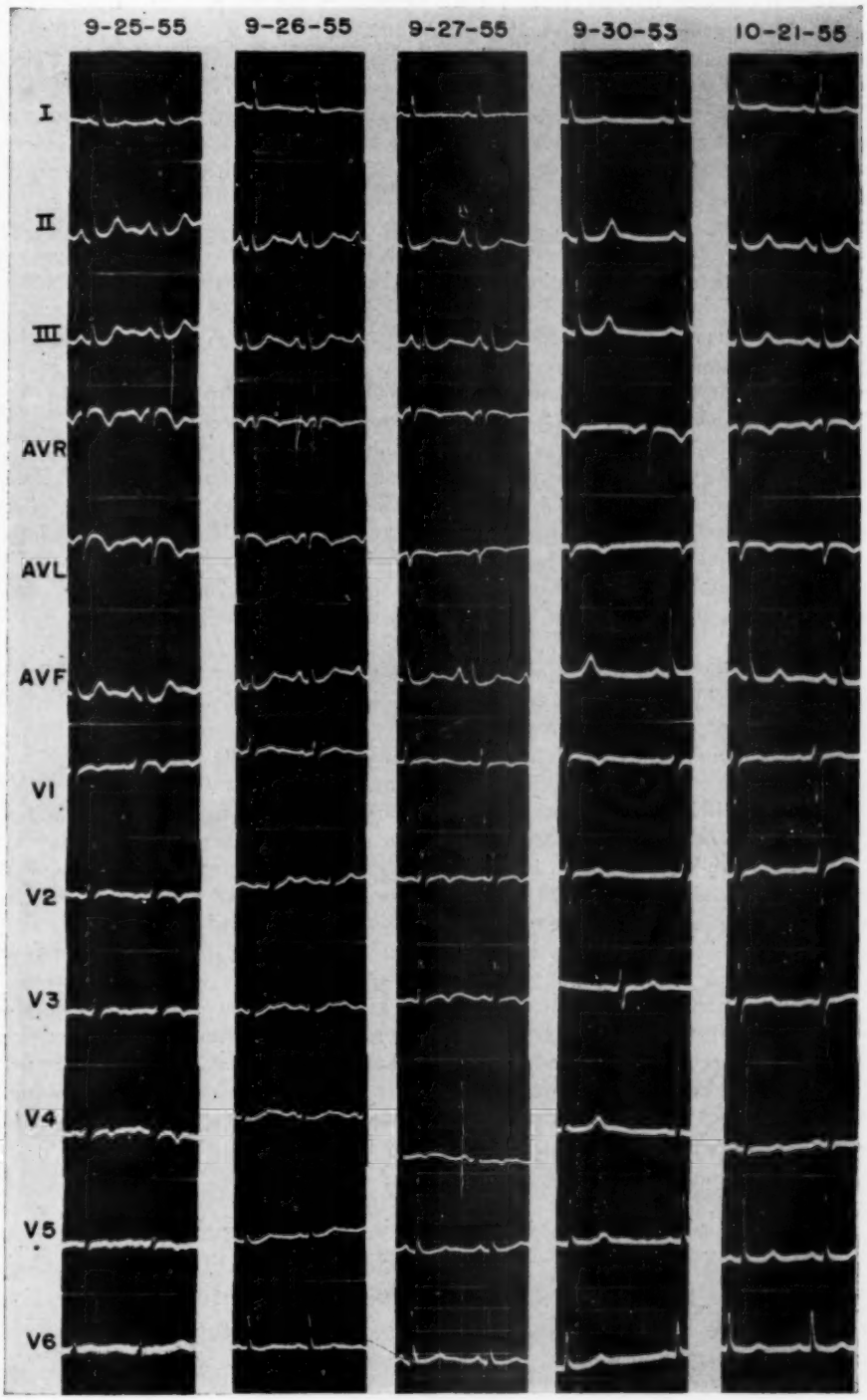

Fig. 2.—Serial ECG study of 51-year-old white man sustaining acute myocardial lesion produced by severe fistblow to the chest. Note especially the T-wave changes in amplitude and direction in the unipolar precordial leads. Minimal, but probably significant, variation in T-wave amplitude is recorded in Lead I.

Oxygen via nasal catheter and morphine sulfate were given for his pain and dyspnea. Subsequent to this therapy, the dyspnea and râles ameliorated rapidly.

We were able then to obtain an elucidative history. The patient had ingested alcohol in quantity and become embroiled in an argument with a passer-by. He was struck on the chest once, directly over the mid-sternum, and knocked to the ground. An extremely painful ache developed in his chest at this time, but he continued on his way to spend the remainder of the evening drinking whiskey. He returned to his room and fell asleep until he was awakened by the acute precordial pain, eight hours after his misadventure.

No specific history of hypertension, rheumatic fever, scarlet fever, diphtheria, diabetes, or venereal disease was obtainable. The patient denied previous episodes of angina, dyspnea, orthopnea, or peripheral edema. A "dumping syndrome" had been present since 1951, sequel to subtotal gastrectomy for chronic gastric ulcer.

The patient's father had died of rectal carcinoma at the age of 68. His mother had died of a "heart attack" at the age of 70.

After receiving emergency treatment in the accident ward, the patient was transferred to the medical service, where his blood pressure was recorded as 148/88 mm. Hg; pulse, 88 per minute; temperature 98.6°F.; respirations, 26 per minute. Extreme tenderness, with a slight amount of crepitation, was noted over the second and third right sternochondral articulations. This pain was accentuated on deep inspiration. Fine, basilar râles were present bilaterally. Cardiac examination revealed the point of maximum impulse to be palpable in the fifth intercostal space in the left mid-clavicular line. Normal sinus rhythm at 88 per minute was present. There were no audible murmurs, friction rubs, or other adventitious sounds. The remainder of the physical examination, including that of the abdomen, extremities, and peripheral pulses, was within normal limits.

An ECG taken in the accident ward, and others during the course of his hospital stay, are illustrated in Fig. 2. The day after admission, portable chest x-rays were taken. These showed clear lung fields and no cardiac abnormalities.

Hospital Course.—Laboratory data: Red blood cells, 3,580,000; hemoglobin, 13.2 Gm.; hematocrit. 41; sedimentation rate (Wintrobe) 27 mm. per hour; white blood cells, 14,000 with normal differential. Urinalysis was normal. Blood urea nitrogen 8 mg. per cent; fasting blood sugar, 107 mg. per cent; total cholesterol 151 mg. per cent with 60 per cent esters; prothrombin level 80 per cent; Lee-White coagulation time, 7 minutes and 8 seconds; Kolmer and VDRL, nonreactive; CO_2 combining power, 23.3 meq.; serum chlorides, 98.8 meq.; serum sodium, 138 meq.; serum potassium, 4.6 meq. The sedimentation rate declined slowly; 14 days after admission it became 12 mm. per hour. The white blood count was then 8,050. C-reactive protein determination was negative.

Only on the second day of hospitalization did a temperature elevation (100° to 101° F.) occur. By the tenth day the chest was normal, cardiac rate was 80 per minute with sinus rhythm, and the sternal tenderness had disappeared. But a harsh, Grade 1 to 2, systolic murmur, heard best at the second right intercostal space, was detected. It persisted throughout the remainder of the patient's hospital stay. He was ambulated gradually after four weeks' bed rest. Discharge was effected five weeks after admission.

SUMMARY

1. Detailed observations upon two individuals suffering the effects of blows producing clinical evidence of myocardial abnormalities are recorded.

2. These are the only instances of myocardial contusion in the English-language literature illustrated by detailed, serial ECG study.

ADDENDUM

Estimation of SGOT (serum glutamic oxalo—acetic transaminase) levels, normally ranging between only 8 and 40 units of activity at 20° C., seems to have provided us with an additional reliable laboratory adjunct in the diagnosis of active destruction of heart muscle. Use of this test should be helpful in evaluating the type of clinical problem we have described.

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Book Reviews

CIRCULATORY DISORDERS. By Erik Warburg, ed. 6, (Vol. IV of NORDISK LAEREBOG I INTERN MEDICIN), Copenhagen, 1956, Glydendal, 413 pages.

Scandinavian medical students use as their standard text *Nordisk Laerebog i Intern Medicin*. This work appears as a series of monographs on the various divisions of internal medicine written by the professors at the Scandinavian medical schools. For many years Professor Erik Warburg has been the author of the volume on cardiology which now appears in its sixth edition.

The approach to the study of heart disease is through pathologic physiology, and the book begins with a general consideration of the factors concerned with heart failure (blood volume, vascular control, blood pressure, etc.). There follows a description of the symptomatology of congestive failure and the methods by which the cardiac patient is examined. Seventy-five pages are devoted to electrocardiography. Vectorcardiography is scarcely mentioned, ballistocardiography not at all.

The "special" part of the book is divided into diseases of the heart and diseases of the arteries.

The section on heart disease follows the traditional sequence of congenital heart disease, coronary artery disease, infectious heart disease, and heart disease in metabolic and endocrine disorders, in deficiency disorders, and in other special conditions. This section also contains brief descriptions of cardiac involvement in unusual conditions, such as leukosis cordis, lymphogranuloma cordis, etc. It ends with a consideration of the cardiac patient in relation to special situations, such as pregnancy, sports, aviation, operation, and with a discussion of digitalis therapy, salt-poor diet, and oxygen therapy.

The section on disease of the arteries begins with a discussion of arterial hypertension in relation to various clinical conditions, including "essential hypertension." There follows a description of the conditions in which the blood pressure is lowered, and finally, a catalogue of unusual arterial disorders such as Takayashus disease, asthenia crurum paraesthetica et dolorosa, and glomus tumors.

Thus, within less than 400 pages the author has condensed essential information covering the entire field of cardiovascular diseases. The presentation of the material is of necessity brief, and somewhat dogmatic, but it is concise, accurate, and up to date. It is of special interest to the American cardiologist because it contains a fairly complete coverage of the contributions of Scandinavian workers. But to the American reader it has two drawbacks; it is written in Danish, and it lacks references, which would be helpful especially where the author has drawn upon the Scandinavian literature. Many of these contributions are theses which are not easily found by American readers.

J. J.

ANESTHESIA FOR SURGERY OF THE HEART. By Kenneth K. Keown, M.D., Springfield, Ill., Charles C Thomas, 1956. Price $3.75.

This 100-page monograph offers a concise, well-organized guide for anesthetists in the handling of patients undergoing surgery for congenital and acquired heart lesions.

The author takes a broad approach to the subject, and describes the development of anesthesia for cardiac surgery, the responsibilities of the anesthesiologist in the choice and preparation of the patient, the diagnosis and treatment of cardiac irregularities, the management of complications, and the postoperative therapy.

The chapter devoted exclusively to anesthetic management of patients entails only 5 pages. Here, general principles are offered without detail concerning specific problems. Anesthetic

technics are described in more detail in subsequent chapters devoted to the various individual heart lesions. Dr. Keown's choice of agents and technics are presented, and reasons for his choice, based on extensive experience, are briefly but adequately stated. In general, they represent widely accepted and well-proved methods.

Many useful tips are included throughout the book, e.g., the use of two cut-down infusions, having two anesthetists for each case, and the continued, direct observation of cardiac action by the anesthetist during open-chest surgery.

No discussion is offered concerning hypothermic technics, or the handling of patients during use of by-pass heart-lung apparatus.

Undoubtedly the greatest value of the monograph lies in the 10 short chapters which give a meaty synopsis of each surgical lesion in its relation to anesthesia and surgery. A chart of the defect is shown, with anatomical and catheterization findings. Then symptoms and essential physiological factors are presented, giving the anesthetist insight into the special problems involved and warning him of the dangers that may occur during operative correction.

This book serves a real purpose in enabling the reader to familiarize himself quickly and clearly with the general requirements and the individual differences of patients facing cardiac surgery.

R. M. S.

MITRAL STENOSIS. By Knud Henning Olesen, Copenhagen, 1955, Ejnar Munksgaard, 228 pages.

Much of the best medical work coming out of Scandinavia is contained in the theses submitted by physicians as a requirement for the degree of M. D., which is comparable to the Ph. D. degree in medicine, granted by some American universities.

The present thesis is a contribution to our knowledge of the course and prognosis of mitral stenosis. It is an attempt to help establish some "background" knowledge for the physician who is consulted regarding the advisability of operation on stenosed mitral valves.

The author points out that systematic clinical examination of the course of rheumatic heart disease during the older decades has been scarce, and mentions the studies of Willius, De Graff and Lingg, Friedmann, Aastrup, and especially Grant, as the only ones which he could find. Therefore, he proceeded to study the progress of 285 patients who had been in a division of the University Hospital of Copenhagen, from 1933 to 1949, and 66 patients from the private files of Dr. Erik Warburg. These cases were all submitted to critical analysis, and the author draws such conclusions as his material will allow for the various groups. The effect of various factors, such as auricular fibrillation, hemoptysis, and pulmonary infarction, is discussed, but the results are too detailed to be repeated in this review. In summary, it may be stated that of 271 adult patients with isolated mitral stenosis, 40 per cent of the women survived 10 years and 18 per cent 20 years after they were first seen; of the men 29 per cent were alive after 10 years and 8 per cent after 18 years.

Altogether, the book is a notable contribution to the natural history of mitral stenosis and it should be a valuable reference work for all who are interested in factors which influence the prognosis of this condition. The book is written in English.

J. J.

Announcements

BRAZILIAN CONGRESS OF CARDIOLOGY AND ANGIOLOGY: The 14th Brazilian Congress of Cardiology and the 5th Brazilian Congress of Angiology will be held in Rio de Janeiro from July 7 to 13, 1957. Information may be obtained from Dr. A. deCarvalho Azevedo, Chairman of the Organization Committee, Rua Domingos Ferreira 28, Rio de Janeiro, Brazil.

UNIVERSITY OF MICHIGAN REGIONAL CONFERENCE ON HYPERTENSION will take place in Ann Arbor, Michigan, June 7-8, 1957, in recognition of the 25th Anniversary of the first production of Experimental Renal Hypertension by Dr. Harry Goldblatt. Reports will be presented on the Basic Mechanisms of Renal Hypertension, including adrenal, neurogenic, and renoprival aspects. Overseas participants will include, among others, Dr. Eduardo Braun-Menendez from Argentina. Participants from the Michigan regional area will include Drs. Goldblatt, Helmer, Wakerlin, Skeggs, Kohlstaedt, Page, Iseri, Kejdi, and McCubbin. Those desiring to attend are urged to write well in advance for information and reservations to Dr. John Sheldon, Director, Department of Postgraduate Medicine, University of Michigan Medical School, University Hospital, Ann Arbor, Michigan.

The 1957 Meeting of the AMERICAN GOITER ASSOCIATION will be held in the Hotel Statler, New York City, on May 28, 29, and 30, 1957. The program will consist of papers and discussions dealing with the physiology and diseases of the thyroid gland.

NATIONAL JEWISH HOSPITAL, at Denver, offers a one-year or two-year FELLOWSHIP IN CARDIO-PULMONARY PHYSIOLOGY, oriented toward academic research. Applications will be accepted from physicians who have completed an internship and at least 2 years of approved residency training in medicine, pediatrics, or surgery. This Fellowship is integrated with the teaching program of the University of Colorado School of Medicine. It is coordinated by Dr. Gardner Middlebrook, Director of Research and Laboratories. The stipend is $6,000 per annum, $3,600 of which is tax free.

Applications will be accepted before July 1, 1957. All inquiries should be addressed to Dr. Goffredo Gensini, Chief, Cardio-Pulmonary Physiology, National Jewish Hospital, 3800 East Colfax Avenue, Denver 6, Colorado.